

# Association of job strain with sleep and psychophysiological recovery in shift working health care professionals



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# **Association of job strain with sleep and psychophysiological recovery in shift working health care professionals**

**Kati Karhula**

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# DOCTORAL DISSERTATION

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## ABSTRACT

**Background.** Social and health care sector employees comprise 16% of the workforce in Finland. In this sector, irregular working hours and stressful work may challenge employees' possibilities to sleep and recover sufficiently. However, empirical evidence on these issues is scarce. Accordingly, the aim of this study was to examine the association of job strain with sleep and psychophysiological functioning and recovery among shift working health care professionals.

**Methods.** As part of the Finnish Public Sector Study, 95 participants were recruited from hospital wards that belonged to the top (high job strain, HJS,  $n=42$ ) or bottom quartiles on job strain (low job strain, LJS,  $n=53$ ) as determined by the average job strain score among the employees of the ward in 2008. These participants experienced job strain at least as high (HJS group) or as low (LJS group) as the average on their ward. Measurements included a modified Trier Social Stress Test (TSST), and a 3-week sleep diary accompanied by an actigraphy to measure the sleep-wake rhythm. The 3-week rosters included three pre-selected, circadian rhythm and recovery controlled measurement days, one morning shift, one night shift and a day off, and the following measurements: ratings of sleepiness (Karolinska Sleepiness Scale), Psychomotor Vigilance Test (PVT), 24h heart rate variability (HRV) measurements and saliva samples of stress biomarkers (cortisol and alpha-amylase).

**Results.** The rosters of the HJS group included more single days off and quick returns than the rosters of the LJS group. Severe sleepiness (KSS score of  $\geq 7$ ) was more common in the HJS group in quick returns. The HJS group reported poorer recovery from all work shifts and after

## ABSTRACT

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morning shifts than the LJS group. High job strain was not associated with extended working hours.

The HJS group had more difficulties in initiating sleep after evening shifts, more often reduced sleep efficiency before morning shifts, and took fewer and shorter naps before the first night shift than the LJS group. Additionally, the HJS group had more often lapses in the PVT during night shifts. Insufficient sleep (31%) and sleep complaints (often 68%) were common in shift workers regardless of the job strain group.

The TSST resulted in, on average, a 2.27-fold increase in cortisol concentration in the HJS group and a 1.48-fold increase in the LJS group (non-significant group difference). The HJS group also had higher salivary alpha-amylase levels 30 minutes after awakening in the morning shift. Apart from that, the salivary cortisol and alpha-amylase levels, profiles and total secretion showed no statistically significant stress group differences. Heart rate and HRV, before and during sleep, were similar in both job strain groups.

**Conclusion.** Shift work contributed to impaired sleep in both the high and low job strain groups, although the sleep impairments were more pronounced in the high job strain group, especially before a morning shift, before and after a night shift and after an evening shift. Associations between job strain and psychophysiological stress-related reactions and recovery were modest or lacking completely. Further intervention studies are needed to determine whether increasing recovery time by reducing the number of quick returns and single days off would also reduce job strain and improve sleep quality among shift workers. Emphasising the importance of sufficient sleep might promote shift workers' recovery and well-being.

## TIIVISTELMÄ

**Johdanto.** Sosiaali- ja terveysalalla työskentelee 16 % Suomen työvoimasta. Terveysalan epäsäännölliset työajat ja kuormittava työ haittaavat riittävää unta ja palautumista, mutta tutkimustuloksia aiheesta on vähän. Tässä tutkimuksessa tavoitteena oli tutkia työstressin yhteyksiä uneen sekä psykofysiologiseen kuormittumiseen ja palautumiseen vuorotyötä tekevillä hoitoalan ammattilaisilla.

**Menetelmät.** Tutkimukseen rekrytoitiin vuoden 2008 Sairaalahenkilöstön hyvinvointi- ja Kunta 10-kyselytutkimuksista 95 osallistujaa. Heidät valittiin työstressin perusteella korkeimman tai matalimman neljänneksen osastoilta. Osallistujien oma arvio työstressistään oli vähintään yhtä korkea korkean työstressin ryhmässä ( $n = 42$ ) ja matala matalan työstressin ryhmässä ( $n = 53$ ) kuin heidän osastonsa keskiarvo. Tutkimukseen sisältyi Trierin psykososiaalinen stressitesti sekä kolmen viikon unipäiväkirja- ja aktigrafiamittaukset uni-valverytmin selvittämiseksi. Kolmen viikon työvuorojaksolla oli kolme etukäteen valittua, vuorokausirytmien ja palautumisen kannalta samanlaista mittauspäivää: aamuvuoro, yövuoro ja vapaapäivä, joiden aikana arvioitiin uneliaisuutta (Karolinska Sleepiness Scale, KSS), mitattiin 24 tunnin sykevälivaihtelua, kerättiin sylkinäytteitä stressin biologisten merkkiaineiden (kortisoli ja alfa-amylaasi) analysoimiseksi ja tehtiin vireystilatestejä (Psychomotor Vigilance Task).

**Tulokset.** Korkean työstressin ryhmän toteutuneissa työvuorossa oli enemmän yksittäisiä vapaapäiviä ja nopeita paluita iltavuorosta aamuvuoroon, joissa korkean työstressin ryhmäläiset myös kokivat enemmän voimakasta päiväaikaista väsymystä ( $KSS \geq 7$ ). Koettu palautuminen

edellisestä työvuorosta ja aamuvuoroista oli heikompaa korkean kuormituksen ryhmässä. Työstressiryhmien välillä ei ollut eroa toteutuneiden työtuntien määrässä.

Korkean työstressin ryhmään kuuluvilla oli enemmän nukahtamisvaikeuksia iltavuorojen jälkeen, tehottomampi uni ennen aamuvuoroja sekä vähemmän ja lyhempikestoisia nokosia ennen ensimmäistä yövuoroa. Korkean työstressin ryhmässä oli myös useammin havaintolipsahduksia vireystilatestissä yövuoron aikana. Lyhentynyt keskimääräinen unen pituus (31 %) ja usein koettu jokin univaikeus (68 %) olivat yleisiä vuorotyötä tekevillä työstressiryhmästä riippumatta.

Trierin stressitestissä syljen kortisolitasot nousivat 2,27-kertaisiksi korkean ja 1,48-kertaisiksi matalan työstressin ryhmässä (tilastollisesti ei-merkitsevä ryhmäero). Korkean työstressin ryhmässä syljen alfa-amylaasitasot olivat korkeampia 30 minuuttia aamuvuoroon heräämisen jälkeen. Muutoin kortisolin ja alfa-amylaasin tasot, profiilit tai kokonaisarvot eivät eronneet työstressiryhmien välillä tilastollisesti merkitsevällä tasolla. Unta edeltävä ja unen aikainen syke ja sykevälivaihtelu olivat samankaltaisia molemmissa stressiryhmissä.

**Johtopäätökset.** Vuorotyön tekeminen oli yhteydessä heikkoon unen laatuun työstressin tasosta riippumatta, vaikkakin korkean työstressin ryhmässä unen laatu heikkeni enemmän ennen aamuvuoroa, ennen ja jälkeen yövuoron ja iltavuoron jälkeen. Työstressin yhteydet psykofysiologisiin stressireaktioihin ja unen aikaiseen palautumiseen olivat vähäisiä tai puuttuivat. Myöhemmissä interventiotutkimuksissa tulisi selvittää, edistäisikö nopeiden työvuoroon paluiden ja yksittäisten vapaapäivien vähentäminen vuorotyöntekijöiden palautumista ja riittävää unta ja vähentäisikö se työstressiä. Edelleen tulisi korostaa hyvän unen merkitystä vuorotyöstä palautumiselle, hyvinvoinnille ja terveydelle.



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Helsinki, 1.12.2014

*Kati Karhula*

## ABBREVIATIONS

ANOVA	one-way analysis of variance
ANS	autonomous nervous system
AUC <sub>g</sub>	area under the curve with respect to ground
AUC <sub>i</sub>	area under the curve with respect to increase
AW	awakening
BMI	body mass index
CAR	cortisol awakening response
CI	confidence interval
ECG	electrocardiography
EEG	electroencephalography
EOG	electro-oculography
ESS	Epworth Sleepiness Scale
EU27	European Union 27 member states
FIOH	Finnish Institute of Occupational Health
FPSS	Finnish Public Sector Study
GLM	general linear model
HF	high frequency component of heart rate variability
HJS	high job strain
HPA	hypothalamus-pituitary-adrenal axis
HR	heart rate
HRV	heart rate variability
IBI	interbeat interval
JC	job control
JCQ	job content questionnaire
JD	job demand
KSS	Karolinska Sleepiness Scale

## ABBREVIATIONS

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LF	low frequency component of heart rate variability
LJS	low job strain
MEQ	morningness-eveningness questionnaire
OR	odds ratio
PASW	Predictive Analytics Software
PSG	polysomnography
PVT	Psychomotor Vigilance Task
REM	rapid eye movement (sleep stage)
RMSSD	root mean square of SD of adjacent R-R intervals
RR	risk ratio
RRI	the interval between two consecutive R-waves in electrocardiography
RT	reaction time
sAA	salivary alpha-amylase
SD	standard deviation
SEM	standard error of mean
SE	sleep efficiency
SNS	sympathetic nervous system
SPSS	Statistical Package for the Social Sciences
TSST	Trier Social Stress Test

## LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following original publications, which are referred to in the text by their Roman numerals. The articles are reprinted with the permission of the copyright holders.

- I Karhula K, Härmä M, Sallinen M, Hublin C, Virkkala J, Kivimäki M, Vahtera J, Puttonen S. 2013. Job Strain, Sleep and Alertness in Shift Working Health Care Professionals – a Field Study. *Industrial Health* 51(4): 406–16.
- II Karhula K, Härmä M, Sallinen M, Hublin C, Virkkala J, Kivimäki M, Vahtera J, Puttonen S. 2013. Association of job strain with working hours, shift-dependent perceived workload, sleepiness and recovery. *Ergonomics* 56(11): 1640–51.
- III Karhula K, Henelius A, Härmä M, Sallinen M, Lindholm H, Kivimäki M, Vahtera J, Puttonen S. 2014. Job strain and vagal recovery during sleep in shift working health care professionals. *Chronobiology International* 31(10): 1179–89.
- IV Karhula K, Härmä M, Sallinen M, Lindholm H, Hirvonen A, Elovainio M, Kivimäki M, Vahtera J, Puttonen S. 2014. Association of job strain with cortisol and alpha-amylase among female shift workers in laboratory and field. *Biological Research for Nursing* [accepted for publication].

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# **1 INTRODUCTION**

Psychosocial factors have emerged as an occupational health issue (Malard et al., 2013). Prevalence of work-related stress has increased in Europe, currently involving a fourth of all employees; similarly the number of and duration of sickness absence due to work-related stress have increased (Houdmont, Kerr, & Addley, 2012). Stress is associated with various symptoms such as sleep disturbances, insomnia (Morin, Rodrigue, & Ivers, 2003; Åkerstedt, 2006) and gastro-intestinal problems (Bhatia & Tandon, 2005). Long-term exposure to stress may also increase the risk of disability pensioning (Mäntyniemi et al., 2012) and diseases such as coronary heart disease (Kivimäki et al., 2012) and depression (Bonde, 2008; Siegrist, 2008). Among shift workers, long-term stress may increase the probability of a co-manifestation of several individual health risk factors, such as a sedentary lifestyle, high blood pressure and cholesterol levels that, in the long run, predispose to a chronic disease (Härmä, Kompier, & Vahtera, 2006).

In Finland, the proportion of social and health care personnel comprise 16% of the total national employed work force (Laine & Kokkinen, 2013). In 2013, 52% of members of the Union of Health and Social Care Professionals (Tehy) and 86% of members of the Finnish Union of Practical Nurses (SuPer) reported working shifts, as opposed to regular day work (The Finnish Confederation of Professionals STTK, 2013). The stressfulness of the nursing profession is well established (Edward et al., 2014; Fischer et al., 2006; Hughes & Rogers, 2004; Johnson, Croghan, & Crawford, 2003; Lim, Bogossian, & Ahern, 2010; McVicar, 2003; Roberts & Grubb, 2014). Prevalence of occupational stress is one of the highest in nursing compared to other sectors (Perkiö-Mäkelä & Hirvonen, 2013; Smith et al., 2000). Working as a nurse is intense,

decision-rich and includes changing clinical environments (Lothschuetz Montgomery & Geiger-Brown, 2010) with frequent interruptions during tasks (Geiger-Brown & Trinkoff, 2010a). Staff retention and intentions to leave the job are common among nursing professionals. When 13 countries were compared, Finland had one of the highest proportion of nurses who intended to leave their job (Aiken et al., 2013).

Sufficient sleep is considered to be one of the pillars of good health along with a healthy diet and regular exercise (Lockley, 2010). Sleep is essential for the recovery from job strain and psychosocial stress. However, workers in the modern 24/7 society can very easily become sleep deprived (Cappuccio, Miller, & Lockley, 2010a; Ferrara & De Gennaro, 2001). Approximately one third of the Finnish population suffers from temporary sleep difficulties (Kronholm et al., 2008). Job strain is suggested to impair sleep more among shift workers than among day workers, because shift workers are also exposed to circadian misalignment. Working shifts is associated with shortened or disturbed sleep for workers on morning and night shifts; problems falling asleep in association with quick returns; and problems waking up too early during the daytime sleep after a night shift (Axelsson et al., 2004; Bonnefond et al., 2006; Härmä, 2006; Tucker et al., 2000). As a result of accumulated research results on the adverse effects of non-typical working times, Finnish legislation ("laki työturvallisuuslain muuttamisesta 329/2013 [Law concerning the change of Occupational Safety Act 329/2013]," 2013) requires a risk assessment of the risks associated with working times.

Few studies to date have examined the links between job strain, sleep, biomarkers of stress and psychophysiological recovery, with salivary cortisol, salivary alpha-amylase and heart rate variability in shift workers within a single analytic setting, which is the focus of this dissertation. The literature review of the thesis presents the prevalence and health effects of job strain and shift work, reviews sleep quantity and quality studies among shift workers and looks through the relevant psychophysiological job strain and recovery measurements.

## **2 REVIEW OF THE LITERATURE ON JOB STRAIN AND SHIFT WORK**

### **2.1 Work stress**

#### **2.1.1 Work stress definitions**

In broad terms, psychosocial hazards at work include job content, workload and pace, job control, work schedules, organizational culture, interpersonal relationships at work, role in the organization and the home-work interface (Rydstedt & Devereux, 2013). Work-related stress is defined as the emotional and psychophysiological reactions to adverse and noxious aspects of work, work environment and work organization by The Advisory Committee for Safety, Hygiene and Health Protection (Rydstedt et al., 2008). Work stress is a state characterized by high levels of arousal and distress which can lead to a variety of emotional, cognitive, behavioural and physiological reactions (“Report on the implementation of the European social partners’ Framework Agreement on Work-related stress,” 2011).

The most common causes of work stress in the Finnish working life are time pressure and deadlines, and both are more common in Finland than in other Nordic countries or the EU27. Other common causes of work stress include overtime work and irregular working hours, poor inter-personal relationships and lack of support from colleagues and supervisors (Vartia et al., 2012).

### 2.1.2 Work stress models

Work stress can be conceptualized in many ways. In this thesis the focus is on job strain, rather than other concepts of work stress and therefore the Job Strain Model (Karasek & Theorell, 1990) is presented in more detail. However, in order to provide a wider perspective of the area some other main models of work stress are touched upon in the next chapter.

#### The Job Strain Model

Job strain has been given particular attention in psychosocial stress research. It is the most widely validated conceptualisation of work stress (Rydstedt & Devereux, 2013). The Job Strain Model, which was developed by Robert Karasek (1979), proposes that job strain occurs when job demands are high and job decision latitude (control over job content) is low (Karasek & Theorell, 1990) (Figure 1). The model argues that work stress and the resulting physical and mental health effects of work stress result, “not from a single aspect of the work environment, but from the joint effects of the demands of a work situation and the range of decision-making freedom (discretion) available to the worker facing those demands”. Job control of decision latitude comprises two related but distinct components: task authority reflects the employee’s authority to make decisions at work whereas skill discretion refers to the level and variety of skill required for the work tasks and the long-term opportunities to acquire new skills at work (Rydstedt & Devereux, 2013).

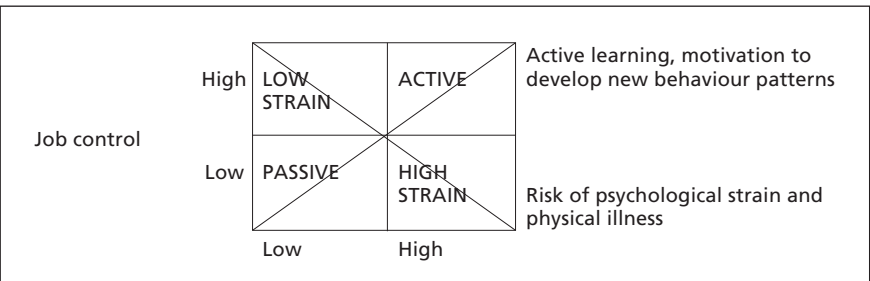


Figure 1. Job demand-job control -model. Adapted from Karasek & Theorell (1990, 32).

Job strain is studied using the Job Content Questionnaire (JCQ), which is widely used as a method for psychosocial job assessment (Karasek et al., 1998; Martin, Salanova, & Peiro, 2007) across nations and occupations (Karasek et al., 1998). The JCQ has a total length of 49 items with three major scales: the first is decision latitude or job control, the second is psychological job demands and the third is workplace social support. There are also subscales for decision latitude, such as skill discretion and decision authority (Maizura, Masilamani, & Aris, 2009).

### **The Effort-reward imbalance -model**

In “the Effort-reward imbalance -model” efforts refer to demands and obligations at work, such as time pressures and task difficulty. Rewards include incentives such as salary, job security and career development opportunities. An effort-reward imbalance may occur if efforts are not rewarded. This will cause work stress in the majority of employees and may lead to increased health problems. Originally the effort-reward imbalance was discovered and used to predict cardiovascular events in blue-collar workers. (Siegrist, 1996.)

### **The Organizational injustice -model**

The model of organizational injustice was developed by Elovainio, Kivimäki & Vahtera (Elovainio et al., 2002). It consists of a scale for procedural justice and a scale for relational justice, adopted from Moorman (1991). Procedural injustice refers to the extent to which decision-making procedures, including input from affected parties, are consistently applied, and the extent to which bias is suppressed, accurate, correctable and ethical. The relational component includes polite, considerate and fair treatment of individuals. Perceiving low justice increases the probability of sickness absences, minor psychiatric disorders and poor self-rated health. (Elovainio et al., 2002.)

### **2.1.3 Prevalence of job strain**

Prevalence of work-related stress has increased in Europe, and now affects more than a quarter of employees (Houdmont et al., 2012). In the

latest European Working Conditions Survey (EWCS) it was found that some psychosocial work factors in particular had deteriorated in the 2010 survey compared to 2005. These factors included job insecurity, skill discretion and decision latitude (Malard et al., 2013).

In Finland, 28% of employees reported high or a relatively high perceived mental workload in the latest Working in Finland -survey (Kivekäs & Ahola, 2013). In the last decade, the proportion of Finnish employees who rated their mental workload as very strenuous or rather strenuous has somewhat decreased (Figure 2). However, the proportion among social and health care workers has remained higher compared to all employees and higher than all female employees. (Perkiö-Mäkelä & Hirvonen, 2013; Perkiö-Mäkelä et al., 2010; Perkiö-Mäkelä et al., 2006). (Figure 2.)

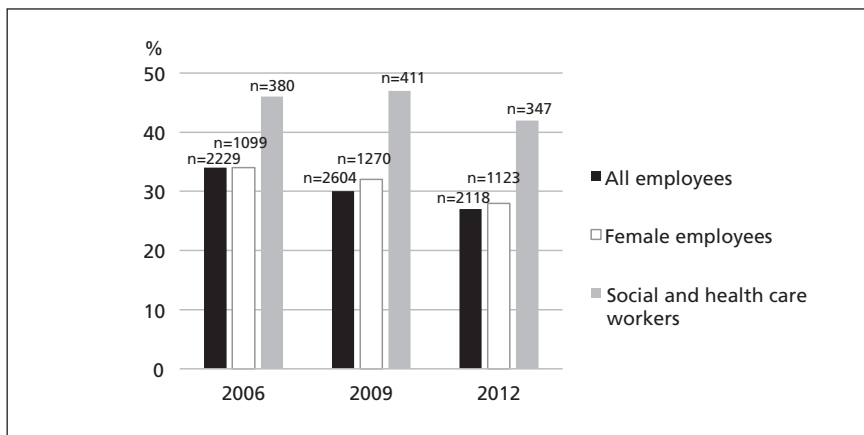


Figure 2. Proportions of Finnish employees rating their mental workload very or rather strenuous. Adopted from Perkiö-Mäkelä & Hirvonen, 2013, Perkiö-Mäkelä et al., 2010, and Perkiö-Mäkelä et al., 2006.

Women are more likely to experience psychological distress than men. Desmarais and Alksnis (2005) suggested that there is a gender difference in the awareness of negative feelings which leads to women expressing and reporting strain more often. Work and family balance may also result in more overall stressors for women leading to increased strain.

### **2.1.4 Health consequences of job strain and its components**

There is strong evidence that job strain, high job demands, low job control, and also, low co-worker or supervisor support, low organizational justice and high effort-reward imbalance predict the incidence of work-related stress disorders (Elovainio et al, 2002; Karasek & Theorell, 1990; Nieuwenhuijsen, Bruinvels, & Frings-Dresen, 2010). According to reviews or meta-analysis (Table 1), employees with high job strain have an increased risk of weight gain (Nyberg et al., 2012), hypertension (Babu et al., 2014; Landsbergis et al., 2013), type 2 diabetes mellitus (Nyberg et al., 2014), coronary heart disease (Kivimäki et al., 2012), and depression (Bonde, 2008; Siegrist, 2008). Moreover, among female workers, stressful work affects reproductive health by increasing the risk of miscarriage, preterm birth, low birth weight and pre-eclampsia (Katz, 2012).

In a Swedish study, both low job control and high job strain have been found to increase the risk of dementia in late life. The hazard ratio was found to be 1.9 and 1.5 respectively (95% CI 1.2–3.0; 95% CI 1.02–2.2) (Wang et al., 2012). A study by Edwards et al. (2012) showed an increased risk for metabolic syndrome in females with high strain jobs (hazard ratio 2.2, 95% CI 1.0–4.6). Moreover, high job demands among females in both individual and work-unit level increased risk of using antihypertensive medication (OR 1.5, 95% CI 1.0–2.3; OR 1.4, 95% CI 1.0–1.9, respectively) (Daugaard et al., 2014).

**Table 1. Job strain and health outcomes according to reviews or meta-analysis.**

Author, year	Studies included	N (male/female)	Main result	Note
<i>Hypertension</i>				
Babu, G. R. et al., 2014	9 cohort or case-control studies	25 799 (NA <sup>1</sup> )	OR <sup>2</sup> 1.3 (95% CI 1.14–1.48)	
Landsbergis, P. et al., 2013	29 cross-sectional, case-control or longitudinal studies	5 581 (51/49%)	systolic BP <sup>3</sup> +3.43 mmHG (95% CI 2.20–4.84), diastolic BP +2.07 mmHG (95% CI 1.17–2.97)	22 studies included in quantitative meta-analysis
<i>Overweight</i>				
Nyberg, S. T. et al., 2012	13 European cohort studies	161 746 (49/51%)	BMI <sup>4</sup> 30.0–34.9 OR 1.07 (95% CI 1.02–1.12), BMI >35 OR 1.14 (95% CI 1.01–1.28)	
<i>Type 2 diabetes mellitus</i>				
Nyberg, S. T. et al., 2014	13 European cohort studies	124 808 (43/57%)	HR <sup>5</sup> 1.15 (95% CI 1.06–1.25)	
<i>Coronary heart disease (CHD)</i>				
Kivimäki, M. et al., 2012	13 European cohort studies	197 473 (51/49%)	HR 1.23 (95% CI 1.02–1.32)	
<i>Depression</i>				
Bonde, J. P., 2008	16 company or population based studies	236 432 (NA)	RR <sup>6</sup> for major depressive disorder and high JD <sup>7</sup> 1.31 (95% CI 1.08–1.59) or JC <sup>8</sup> 1.20 (95% CI 1.08–1.39) (7 studies)	clinical criteria of depression was used in 7 studies
Siegrist, J., 2008	12 prospective studies with middle-aged population	133 008 (NA)	summary OR estimate 1.8	JC/JD or ERI-model
<i>Reproductive health</i>				
Katz, V. L., 2012	32 studies	> 1 000 000 pregnancies (-/100%)	miscarriage (RR 1.5), preterm birth (RR 1.22–1.63), low birth weight (RR 1.37–2.2)	outcome measure occupational fatigue

<sup>1</sup> not applicable, <sup>2</sup> odds ratio, <sup>3</sup> blood pressure, <sup>4</sup> body mass index, <sup>5</sup> hazard ratio, <sup>6</sup> risk ratio, <sup>7</sup> job demand, <sup>8</sup> job control



It is difficult to develop monetary estimates of stress-related losses (Karasek & Theorell, 1990), but consequences of job strain are also an important economic issue (Sultan-Taieb et al., 2013). The number of sickness absences and their duration due to work-related stress has increased (Houdmont et al., 2012). According to European statistics, over 50% of sickness absences are related to work stress and other psychosocial factors (European Agency for Safety and Health at Work, 2014). Long-term exposure to job stress also increases the risk of disability pensioning (Laine et al., 2009; Mäntyniemi et al., 2012), in females with an OR of 1.7 (95 % CI, 1.3–2.2) (Canivet et al., 2013). Conservative estimates suggest that stress accounts for approximately 30% of the overall costs of illness and accidents, totalling 0.5–3.5% of the gross domestic product across Western European nations (Nater, Skoluda, & Strahler, 2013).

### **2.2 Shift work**

Shift work is defined as a work schedule in which a worker replaces another on the same job within a 24 hour period (Knutsson, 2004; Åkerstedt & Wright, 2009). Usually shift work covers a wide range of working time arrangements (Knutsson, 2004; Sallinen & Kecklund, 2010): regular 3-shift systems, irregular 3-shift systems, 2-shift systems, permanent night work and shift systems during extended operations, for example medical interns or offshore operations (Sallinen & Kecklund, 2010). Rotating shift systems dominate in Europe (Åkerstedt & Wright, 2009). In the Finnish health care sector, shift arrangements are typically 8 hours for daytime shifts and 10 hours for night shifts, whereas 12 hour shifts are more common, for example, in the USA (Rogers et al., 2004).

#### **2.2.1 Prevalence of shift work**

The prevalence of shift work is typically over 20% in industrialized societies (Åkerstedt & Wright, 2009) and was 22% in Finland in the latest Working in Finland -survey (Kandolin & Tuomivaara, 2013). The prevalence of three shift work is somewhat higher in the health care sector than on average, with varying prevalence in different western countries. In Finland, 52% of members of the Union of Health and Social Care

Professionals (Tehy) and 86% of the members of the Finnish Union of Practical Nurses (SuPer) reported undergoing work other than regular day work (The Finnish Confederation of Professionals STTK, 2013), which is comparable to over 70% of shift workers in the Finnish Public Sector Study (Kivimäki et al., 2006).

In Sweden, 25% of nurses had experienced three-shift work one year after graduation (J. Axelsson personal information 7.10.2013). In a Dutch sample with the majority of nurses working in elderly care, 74% worked a three shift work (Peters, de Rijk, & Boumans, 2009), but according to personal information from the author, in general 33% of nurses in the Netherlands work a three-shift work in elderly care (V. Peters personal information 7.10.2013). In Canada, slightly under 40% among female health care professionals were three-shift workers (Demers, Wong, & McLeod, 2010). Also in the United States approximately 40% of registered nurses had a non-standard shift work (NIOSH, 2010).

### **2.2.2 Favourable shift schedules**

Forward-rotating shift systems are favourable in preference to backward-rotating systems (Driscoll, Grunstein, & Rogers, 2007; Sallinen & Kecklund, 2010). (Table 2.) Forward rotation disturbs sleep less because of the natural tendency of the circadian clock to delay (Åkerstedt & Wright, 2009). Backward rotation includes quick returns, where an evening shift is immediately followed by a morning shift. Quick returns are the most burdensome combination of shifts, because recovery times between shifts are too short and thus cause fatigue (Kandolin & Huida, 1996). The number of consecutive night shifts should be low and early morning shifts should be avoided (Kandolin & Huida, 1996), because daytime sleep after a night shift does not seem to improve much between consecutive night shifts (Åkerstedt & Wright, 2009). In the event of an early morning shift, the phase advance of the early work start time is not compensated by a corresponding phase advance of going to bed earlier in the evening (Åkerstedt, Kecklund, & Selen, 2010). In Finnish hospitals, the shift schedules are traditionally only planned three weeks in advance. Shift systems are irregular and therefore work schedules have an adverse effect on work-family balance and social life (Kandolin & Huida, 1996).

**Table 2. Example of a fast forward rotating and a slow backward rotating shift system in three-shift work. M = morning shift, E = evening shift, N = night shift, - = day-off. Adopted from Hakola & Härmä, 2001.**

	Mon	Tue	Wed	Thu	Fri	Sat	Sun	Mon	Tue	Wed	Thu	Fri	Sat	Sun
Fast forward rotating system														
Employee 1	M	M	E	E	N	N	-	-	-	-	M	E	E	N
Employee 2	-	-	M	M	E	E	N	N	-	-	-	M	M	E
Employee 3	-	-	-	-	M	M	E	E	N	N	-	-	-	M
Employee 4	N	N	-	-	-	-	M	M	E	E	N	N	-	-
Employee 5	E	E	N	N	-	-	-	-	M	M	E	E	N	N
Slow backward rotating shift system														
Employee 1	E	E	E	E	-	M	M	M	M	-	N	N	N	E
Employee 2	-	M	M	M	M	-	N	N	N	N	-	-	-	E
Employee 3	M	-	N	N	N	N	-	-	-	-	-	E	E	M
Employee 4	N	N	-	-	-	-	-	-	E	E	E	E	-	N
Employee 5	-	-	-	-	E	E	E	E	-	M	M	M	-	-

Internationally, relatively many studies (Borges & Fischer, 2003; Geiger-Brown & Trinkoff, 2010a; Geiger-Brown & Trinkoff, 2010b; Gillespie & Curzio 1996; Hakola, Paukkonen, & Pohjonen, 2010; Korompeli et al., 2013; Rogers et al., 2004; Takahashi et al., 1999) have explored work times in the health care sector, but many of these studies (Borges & Fischer, 2003; Geiger-Brown & Trinkoff, 2010a; Geiger-Brown & Trinkoff, 2010b; Gillespie & Curzio 1996) have investigated the differences between 8- and 12-hour shifts or even 16-hour long night shifts (Takahashi et al., 1999). It is common to work for over 8 hours a day (Trinkoff et al., 2006) and also to have extended (>12h) work shifts (Geiger-Brown et al., 2012; Sallinen & Kecklund, 2010) in the health care sector. Therefore long, over 35–40 hour working weeks are common among nursing personnel (Trinkoff et al., 2006). Several studies (de Castro et al., 2012; Rogers et al., 2004; Scott et al., 2006; Wu et al., 2013) have established the prevalence of long working hours among health care staff. Scott et al. (2006) found that in 86% of the shifts nurses worked longer than scheduled. Rogers et al. (2004) found that 40% of the total of over 5 000 work shifts exceeded 12 hours. In the United States, up to 11% of nurses worked longer than a 16 hour work shift at least once in four weeks. Notably, shifts longer than 12.5 hours increase the prevalence of incidents of nodding off at work (4 vs. 1% <8,5h) (Scott et al., 2006).

In health care organizations, the direction or speed of the shift rotation, the irregularity of the shift system and the employees' influence on her own working hours has not been studied as extensively as the shift length. Previous studies show that nurses and eldercare workers rate their influence over working hours as poor (Aiken et al., 2001; Nabe-Nielsen et al., 2010). In an extensive international study (Aiken et al., 2001) the percentage of nurses that could participate in their scheduling ranged from less than a third in Canada to over two thirds in Germany. Low control over working times has negative consequences. Among Finnish municipal employees, female employees in the lowest quartile on working time control had an OR of 1.6 (95% CI 1.3–2.0) for psychological distress and an OR of 1.8 (95% CI 1.5–2.3) for poor health (Ala-Mursula et al., 2002). Employees working overtime without the opportunity to regulate their working hours display more symptoms of distress and more often face work-family conflicts than employees who can flexibly

arrange their working hours (Kandolin & Härmä, 2001). On the other hand, it is possible that “self-scheduling” work shifts results in increased fatigue risk (Lothschuetz Montgomery & Geiger-Brown, 2010). In a Finnish study, after a 6 months intervention with a forward rotating shift system with less quick returns, the majority of nurses preferred the previous strenuous backward rotating shift system that provided longer continuous leisure time (Kandolin & Huida, 1996).

There is little research on how nurses recover from different work shifts and how they use individual fatigue countermeasures. A recent review (Åkerstedt & Wright, 2009), did not find any randomized controlled studies on any shift system categories and there is also a shortage of controlled intervention studies. With observational studies one can identify the most problematic shift characteristics and then indirectly infer which of the possible rescheduling options would likely result in marked positive changes in sleep and sleepiness (Sallinen & Kecklund, 2010).

### **2.2.3 Health consequences of shift work**

Shift work has been associated with various symptoms and adverse health effects. Especially after starting shift work, the risk of psychophysiological symptoms, like sleep disturbances and digestive problems, is elevated (Taylor, Briner, & Folkard, 1997). Up to 20% of shift workers change to a day job during the first twelve months after starting shift work (Härmä, 1993).

Work hours that displace sleep to the day time and work to the night time interfere with the circadian and homeostatic regulation of sleep (Åkerstedt & Wright, 2009). Shift work that includes night work in particular results in negative effects on sleep (Konturek, Brzozowski, & Konturek, 2011; Åkerstedt & Wright, 2009), subjective and physiological sleepiness, performance (Åkerstedt & Wright, 2009) and an increased accident (Åkerstedt & Wright, 2009) or occupational injury risk (Lombardi et al., 2010). For example, the risk of injury increases during consecutive night shifts, being 17% higher on the third night and 36% higher in the fourth night compared to the first one (Folkard, Lombardi, & Tucker, 2005). Among nurses, being a night worker increases the risk of insomnia (OR 1.48, 95% CI 1.10–1.99) and chronic fatigue (OR 1.78, 95% CI 1.02–3.11) (Øyane et al., 2013).

**Table 3. Shift work and health outcomes according to reviews or meta-analysis.**

<b>Author, year</b>	<b>Studies included</b>	<b>N (male/female)</b>	<b>Main result</b>	<b>Note</b>
<i>Hypertension</i>				
Esquirol, Y. et al., 2011	28 <sup>1</sup> (a total of 30 studies)	96 767 (63/37%) <sup>2</sup>	29% of studies found positive, 61 % negative and 11 % inconsistent association	blood pressure variability studies excluded by the author
<i>Overweight</i>				
Amani, R. & Gill, T., 2013	8 cross-sectional or cohort studies on obesity and/or BMI	32 762 (NA) <sup>3</sup>	6/8 studies found a positive association	
<i>Metabolic Syndrome</i>				
Canuto, R., et al., 2013	10 cross-sectional, case-control or longitudinal studies	41 652 (NA)	8/10 studies found a positive association	insufficient evidence due to various confounders
<i>Type 2 diabetes mellitus</i>				
Gan, Y. et al., 2014	12 studies	226 652 (NA)	OR 1.09 (95% CI 1.05–1.12), men OR 1.37 (95% CI 1.20–1.56), women OR 1.09 (95% CI 1.04–1.14)	
<i>Cardiovascular events</i>				
Vyas, M. V. et al., 2012	34 studies	2 011 935 (NA)	myocardial infarction RR 1.23 (95% CI 1.15–1.31, any coronary event <sup>4</sup> RR 1.24 (95% CI 1.10–1.39)	

Author, year	Studies included	N (male/female)	Main result	Note
<i>Breast cancer</i>				
Ijaz, S. et al., 2013	12 case-control and 4 cohort studies	1 444 881 (~100%)	case-control studies RR 1.09 (95% CI 1.02–1.20), cohort studies RR 1.01 (95% CI 0.97–1.05)	insufficient evidence based on low quality of exposure data
Jia, Y. et al., 2013	8 case-control and 5 cohort studies	197 044 (~100%)	case-control studies RR 1.32 (95% CI 1.17–1.50), cohort studies RR 1.08 (95% CI 0.97–1.21)	additional epidemiological studies are needed
<i>Reproductive health</i>				
Stocker, L. J., et al., 2014	15 independent cohort studies	123 403 (~100%)	adjusted OR for infertility 1.11 (95% CI 0.86–1.44, 1.61%) and early spontaneous pregnancy loss adjusted OR 1.41 (95% CI 1.22–1.63)	

<sup>1</sup> selected by the author  
<sup>2</sup> in 24/28 studies providing gender proportions  
<sup>3</sup> not applicable  
<sup>4</sup> cardiovascular events, coronary mortality, cerebrovascular mortality, cardiovascular mortality or all-cause mortality

Shift work is associated with the risk of various diseases and adverse health effects (Åkerstedt & Wright, 2009). In recent reviews and meta-analysis (Table 3), shift work has been associated with an increased risk of hypertension (Esquirol et al., 2011), obesity (Amani & Gill, 2013), metabolic syndrome (Canuto, Garcez, & Olinto, 2013), type 2 diabetes (Gan et al., 2014), myocardial infarction, coronary events (Vyas et al., 2012), infertility, early spontaneous pregnancy loss (Stocker et al., 2014) and breast cancer (Jia et al., 2013). However, another concurrent review (Ijaz et al., 2013) on the association of shift work and breast cancer found insufficient evidence of the association where a single study (Grundy et al., 2013) demonstrated an increased risk only for long-term night shift workers (OR 2.21, 95% CI 1.14–4.31).

Single studies show some additional results on health outcomes and shift work. Shift workers are more likely to have symptoms of metabolic syndrome i.e. visceral obesity, dyslipidaemia, elevated blood pressure, and serum glucose levels, than day workers (OR 1.78, 95% CI 1.03–3.08) (Tucker et al., 2012). Shift work has been associated with an elevated risk of rheumatoid arthritis in females (HR 1.33, 95% CI 1.01–1.75) (Puttonen et al., 2010) and permanent night shift work is associated with a risk of miscarriage (RR 1.6, 95% CI 1.3–1.9) (Whelan et al., 2007).

In shift work research, it is important to notice that there is a “healthy worker effect”, referring to a selection process that leads to a workforce of shift workers who are healthier than the general population or day workers (Knutsson, 2004). The potentially disadvantageous effects of shift work are underestimated if the workers moving from shift work to day work are not included in the data (Kivimäki et al., 2001; Knutsson, 2004). The “healthy worker effect” has been dealt with in some studies by subdividing the study sample into day workers, current shift workers and former shift workers (Puttonen, Viitasalo, & Härmä, 2012). However, this division does not take into account the selection that occurs before employment (Knutsson 2004). According to an epidemiologic estimation of fatalities related to occupational factors, shift work and job strain increase mortality by over 400 persons per year in Finland (Nurminen & Karjalainen, 2001).



## **3 REVIEW OF THE LITARATURE ON SLEEP**

### **3.1 Sleep quantity and quality**

Sleep is important for health and functional capacity (Sallinen & Kecklund, 2010; Spiegel, Leproult, & Van Cauter, 1999) and sleep is increasingly considered as one of the pillars of good health, along with a healthy diet and frequent exercise (Lockley, 2010). During the past hundred years, there has been a steady decline in the average sleep duration due to various environmental and social reasons, for example, the 24/7 society and extended shift work (Cappuccio, et al., 2010a).

A good night's sleep equates to at least 6 hours and ideally 8 hours of continuous sleep, with changes in sleep duration or continuity being associated with negative impacts on alertness and health outcomes. Approximately three-quarters of men and women sleep 6–8 hours per night. (Cappuccio et al., 2010a.) Adult women have reported to sleep consistently less than men up to the age of 50–55 years (Cappuccio et al., 2010a), although in the Finnish general population, the average self-reported sleep duration is 7.5 hours, for women 7.6 hours and for men 7.4 hours (Kronholm et al., 2006).

Stress, in general, has a negative effect on sleep (Elovainio et al., 2009; Groeger, Zijlstra, & Dijk, 2004; Lallukka et al., 2010; Vahtera et al., 2010). Sleep and stress seem to be counterparts that affect each other. For example, stress increases arousal and sleep decreases it; stress disturbs homeostasis and sleep is important in maintaining it. (Hasson & Gustavsson, 2010.) The negative effect of stress on sleep has been supported by cross-sectional questionnaire studies among daytime workers (Kompier, Taris, & van Veldhoven, 2012). For example, in a study by

Kalimo et al. (2000), the prevalence of disturbed sleep was 30% among the high-strain workers compared to 5% among the low-strain workers. Shortened sleep is also associated with extended working hours (>41h/week) (Krueger & Friedman, 2009). In nurses, greater job stress was associated with poorer reported sleep quality (Lin et al., 2014).

For a shift worker the “opportunity for sleep -factor” is pronounced compared to a day worker (Axelsson, Kecklund, & Sallinen, 2010). Sleeping outside the circadian “window” causes difficulties in falling asleep if sleep occurs too early, or difficulties maintaining sleep if the sleep opportunity is too late (Lockley, 2010). On average, sleep before an early morning shift is shortened by 2–4 hours compared to habitual sleep length (Sallinen & Kecklund, 2010), and daytime sleep after a night shift is shortened by 1–4 hours (Åkerstedt & Wright, 2009). Daytime sleep quality is also poor, because high morning cortisol levels and low melatonin levels promote wakefulness (Kudielka et al., 2007; Lac & Chamoux, 2004).

Nurses also sleep longer on a day off than on a work day (Dorrian et al., 2006; Garde, Hansen, & Hansen, 2009). The lowest sleep quality has been observed in nurses working mixed shifts, including night shifts (Garde et al., 2009). On the other hand, nursing students have been found to tolerate their first night shift period very well, with only a small decline in the main sleep period (Fietze et al., 2009).

## **3.2 Sleepiness, sleep deprivation and sleep disturbances**

Sleepiness is simply defined as “the tendency to fall asleep” (Carskadon & Dement, 1982). Notably, excessive daytime sleepiness is defined as “being sleepy when one is not expected to be sleepy” (Arand et al., 2005). Relatively less is known about sleepiness than about sleep (Åkerstedt, 2010). Under normal conditions, daytime functioning is relatively stable during the day. There is a wake-dependent decline towards the end of the day. (Lockley, 2010.) In a recent study (Flo et al., 2013) 70% of three-shift working nurses were often tired or sleepy at work. Similarly, almost two thirds of critical care nurses had to struggle to stay awake at least once in a 4-week study period (Scott et al., 2006).

Sleep disturbances and sleep deprivation are common in modern society (Cappuccio et al., 2010a; Ferrara & De Gennaro, 2001). Sleep deprivation is in question when the amount of sleep is markedly shorter than the actual sleep need. Sleep disturbances include difficulties in initiating sleep, difficulties in re-initiating sleep after waking up, waking up too early, feeling tired after a normal night sleep and a strong day-time sleepiness after a normal night sleep (AASM, 2001).

Acute sleep deprivation causes sleepiness and affects mood, alertness and performance (Bonnet, 2011). Chronic partial sleep deprivation has its effects on many bodily functions, for example, sympathetic activity and glucose intolerance increases (Spiegel et al., 1999). Cognitive functions decline and it has been shown that sleep-deprived people underestimate the cognitive impact (Banks & Dinges, 2011, Haavisto et al., 2010). Alterations in metabolic and endocrine functions can be seen in less than a week's sleep restriction (Spiegel et al., 1999) and in the long run the alterations increase the risk of, for example, obesity and cardiovascular diseases (Kivimäki et al., 2001; Sabanayagam & Shankar, 2010). Both short (<4/5/6/7 hours) and long sleep durations (>8/9/10/12 hours) are associated with increased all-cause mortality (Cappuccio et al., 2010b).

Approximately one third of the Finnish general population report insomnia or disturbed sleep (Kronholm et al., 2008). When occurrence of sleep difficulties is compared to the general population, night shift work nurses report double (Flo et al., 2013) or nearly triple the occurrences (Lin et al., 2014) of poor sleep. Sleep fragmentation, i.e. periodic arousals from sleep, reduces the restorative power of sleep and causes similar deficits as sleep deprivation (Bonnet, 2011). With increasing age, the structure of sleep changes and sleep becomes more fragmented (Carrier et al., 1997; Gander & Signal, 2008), which may impair the ability to maintain good sleep, especially in shift workers (Gander & Signal, 2008).

### **3.3 Naps as a fatigue countermeasure**

Despite the irregular sleeping hours, shift workers need to operate well when on duty (Takeyama, Kubo, & Itani, 2005). Napping is an effective fatigue countermeasure, especially prior to (Tremaine et al., 2013) or during night shifts (Bonnefond et al., 2001; Davy & Gobel, 2013;

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Ruggiero & Redeker, 2014). Scheduled napping on duty resulted, for example, in reduced levels of subjective sleepiness, shortened response time and improved performance (Davy & Gobel, 2013). On the other hand, if naps are scheduled late in the night shift, they may produce sleep inertia that decreases performance, which manifested as longer reaction times and more lapses in a visual vigilance test compared to a no-nap condition (Kubo et al., 2010).

Among nursing professionals, scheduled napping before a night shift is relatively common. In previous studies, the proportions of intentional or unintentional nightshift nappers have varied remarkably from 3% (Bjorvatn et al., 2012) to 20% (Scott et al., 2006) and even up to half of the nurses (Daurat & Foret, 2004). There are no Finnish published studies on scheduled napping among nurses. In the Finnish health care sector, scheduled napping is generally either not recommended or prohibited.

## **4 REVIEW OF THE LITERATURE ON STRESS PSYCHOPHYSIOLOGY AND RECOVERY**

There are many physiological methods to measure stress, both in the laboratory and in field conditions. Results of stress studies in the laboratory are assumed to reflect the way individuals react in their everyday life (Kidd, Carvalho, & Steptoe, 2014). Psychophysiological biomarkers of stress include sympatho-adrenal biomarkers such as adrenaline and noradrenaline and HPA-axis biomarkers such as cortisol and, prolactin (Chandola, Heraclides, & Kumari, 2010). Saliva is easily collected and therefore studies have focused on the evaluation of salivary cortisol, alpha-amylase, chromogranin A and immunoglobulin A as stress markers (Obayashi, 2013). Heart rate (HR) and heart rate variability (HRV) can be used to measure cardiac autonomic function during work and rest (Togo & Takahashi, 2009). The major stress biomarkers are cortisol and alpha-amylase that can be measured in blood, saliva and urine (Obayashi, 2013). In this study (Study IV), the stress biomarkers used were salivary cortisol and alpha-amylase. Recovery during sleep was measured with HRV. These methods are presented in the following chapters.

### **4.1 Heart rate variability**

Heart rate variability provides a non-invasive technique for indirectly measuring sympathetic and parasympathetic modulation of heart rate (Hall et al., 2007). In electrocardiography (ECG), the time interval between consecutive R waves that correspond to the contraction of the ventricles is called the RR interval (RRI). Heart rate variability reflects

the beat by beat fluctuation of RRIs that are mainly due to changes in activity of the sympathetic and parasympathetic nerves innervating to the sinus node (Togo & Takahashi, 2009). Normally, sympathetic activity increases with different stressors increasing the heart rate (HR) and decreasing the heart rate variability (HRV). Conversely, restful conditions accentuate parasympathetic activity resulting in a decreased HR and an increased HRV (Uusitalo et al., 2011).

Sleep is a crucial physiological element of restoration, and it is associated with parasympathetic dominance (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Sleep is an excellent time to measure parasympathetic nervous system (PNS) function, because HR is under PNS control during supine rest (Stein & Pu, 2012). When HRV is studied during sleep, the extraneous factors influencing HRV are also reduced compared to daytime measurements.

There are two primary approaches for the analyses of HRV; time and frequency domain techniques (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Among the commonly applied time-domain parameters are SDNN, that is, the SD of all normal R-R intervals and RMSSD which stands for the square root of the mean squared differences between adjacent normal R-R intervals. Of the frequency domain measures, the most commonly applied are high frequency power (HF), low frequency power (LF) and LF/HF ratio of the low to high frequency power. (Billman, 2011). HF (0.15–0.4 Hz) represents the respiratory cycle and is mediated by the parasympathetic nervous system. LF (0.04–0.15 Hz) reflects input from both branches of the autonomous nervous system. Sympathetic modulation is, therefore, often input from the ratio of LF to HF components. (Hall et al., 2007.)

Decreased heart rate variability is an independent risk factor for morbidity and mortality (Thayer, Yamamoto, & Brosschot, 2010). Decreased HRV may increase the long-term risk of cardiovascular-related mortality and morbidity (Lo et al., 2010). Only a limited number of studies have examined the associations between heart rate variability and work-related stress (Clays et al., 2011). Among females, a higher effort-reward imbalance was associated with lower HRV (Hintsanen et al., 2007). Other previous studies have found both decreased (Collins, Karasek, & Costas,

2005; Hernandez-Gaytan et al., 2013; van Amelsvoort et al., 2000; Vrijkotte, van Doornen, & de Geus, 2000) and normal HRV (Kageyama et al., 1998; Riese et al., 2004) in connection with job strain. Vrijkotte et al. (2000) found an increased HR reactivity to a stressful workday and a lower 24 hour vagal tone. In another study (Uusitalo et al., 2011) a higher level of irritation during work was associated with lower HRV during sleep the next night. There is indication that among shift workers, decreased low-to-high frequency ratio (LF/HF ratio) is predominantly related to sleep, independent of the night/day cycle (Freitas et al., 1997).

In health care staff working shifts, studies of the associations between job strain and HRV have produced conflicting results. The high frequency HRV was found to be significantly higher during days off compared to working shifts (Chung et al., 2012). Also, their low to high frequency ratio (LF/HF) on days off was found to be lower than that during shift work (Chung et al., 2012). On the other hand, HRV profiles usually return to the baseline level after each shift (Lo et al., 2010). Moreover, when female nurses and care-givers in regular day work and shift work were compared on a day shift, no significant differences in 24 -hour ambulatory HRV were found (Yoshizaki et al., 2013). Järvelin-Pasanen et al. (2013) found no association between perceived occupational stress and HRV for nurses working shifts.

### **4.2 Salivary cortisol**

Cortisol is produced by the adrenal glands and is an essential hormone (Niu et al., 2011) that affects many bodily functions, including metabolism and regulation of the immune system (Lundberg, 2005; Niu et al., 2011). Salivary cortisol is the most frequently measured biomarker of stress (Fries, Dettenborn, & Kirschbaum, 2009) because it is a non-invasive method compared to blood sampling (Kirschbaum & Hellhammer, 2000). Salivary cortisol reflects the amount of free, biologically active fraction of cortisol (Kudielka, Hellhammer, & Wust, 2009).

In healthy individuals, cortisol has a typical circadian profile with a peak shortly after waking up and low levels in the evening (Fries et al., 2009; Wong et al., 2012). The typical cortisol awakening response (CAR) is a 50–100% increase (Chandola et al., 2010; Kirschbaum

& Hellhammer, 2000) in cortisol concentration in about 30 minutes (Fekedulegn et al., 2012; Kirschbaum & Hellhammer, 2000) or 30–45 minutes after waking (Nater et al., 2013). The CAR has a remarkable intra-individual stability (Kirschbaum & Hellhammer, 2000) but a large inter-individual variation (Stone et al., 2001). Cortisol levels also adapt rapidly to regular conditions, for example, at work (Lundberg, 2005).

Altered cortisol secretion is associated with fatigue (Kudielka et al., 2007), depression (Kudielka et al., 2007; Marchand et al., 2014), obesity and immune dysfunction (Kudielka et al., 2007). The studies of cortisol profiles during stress show somewhat conflicting results (Miller, Chen, & Zhou, 2007; Wong et al., 2012). The main finding in a meta-analysis of over 100 studies was that chronic stress lowers the cortisol peak in the morning (CAR, cortisol awakening response) and elevates the level in the evening (Miller et al., 2007). Similarly, a review of CAR and psychosocial factors found that increased CAR was associated with both job strain and general life stress (Chida & Steptoe, 2009). When there is a prolonged exposure to stressors, the body's biological systems may mount a dysregulation (counter-regulatory response) where cortisol rebounds to lower than normal levels (Fekedulegn et al., 2012).

Niu et al. (2011) found only half a dozen previous studies with a focus on shift work and cortisol levels. Night shift workers were found to have a cortisol secretion pattern lower in the morning and higher in the evening compared to permanent day workers (Kudielka et al., 2007; Lac & Chamoux, 2004). However, serum cortisol profiles that follow the typical circadian profile of day workers have also been found among nurses on night shift (Korompeli et al., 2009).

Stressful situations induce profound endocrine responses in the majority of people (Kirschbaum, Pirke, & Hellhammer, 1993). A meta-analysis covering over 200 studies concluded that performance tasks reliably elicit cortisol reactions (Dickerson & Kemeny, 2004). For example, the Trier Social Stress Test (TSST) induces a 2–4 fold increase in salivary cortisol. These cortisol responses are, on average, higher in males than in females (Kirschbaum et al., 1993). With women 50–150% increases from the baseline are usually found (Kudielka et al., 2009).



### 4.3 Salivary alpha-amylase

Salivary alpha-amylase (sAA) is an enzyme produced by salivary glands (Nater et al., 2006), primarily known to initiate the digestion of starch (Nater & Rohleder, 2009). Salivary alpha-amylase has not been studied as extensively as cortisol (Rohleder & Nater, 2009) as the studies have only accumulated during the last 10 years. Activation of the autonomic nervous system (ANS) with a combination of both sympathetic and parasympathetic innervation of the salivary glands leads to high activity of the alpha-amylase (Nater et al., 2006). Salivary AA has a rapid stress responsiveness (Strahler et al., 2010). Acute sAA responses to different stressors do not seem to show either gender differences or changes during the adult life span (Rohleder & Nater, 2009).

A normal diurnal alpha-amylase profile dips after waking up. Exposure to long-term stress is associated with flatter diurnal slopes and a decreased daily production of sAA. (Rohleder & Nater, 2009). However, there are only a few earlier publications on work stress and sAA (Groer et al., 2010; Limm et al., 2011; Wingenfeld et al., 2010; Wong et al., 2012). One of these studies which was conducted among nurses (Wingenfeld et al., 2010), found that the sAA profiles of nurses' working day shifts were not associated with work stress. On the other hand, Wong et al. (2012) carried out a study involving paramedics with a male predominance and found that shift working paramedics had higher job strain and flatter diurnal slopes and a reduced daily production of sAA. Among middle management employees, sAA production was reduced more in the stress management intervention group compared to the control group (Limm et al., 2011).

### 4.4 Psychophysiological recovery from stress

Recovery can be regarded as an opposite process of the psychophysiological activation under stressful situations (Sonnentag & Natter, 2004). In physiology, recovery shows as a decrease of physiological stress markers, such as decreased heart rate and secretion of cortisol and adrenaline (Geurts & Sonnentag, 2006). From psychological perspective, a recovered

individual is capable and ready to continue his/her demand or meet new demands (Zijlstra & Sonnentag, 2006).

Long-term repeated stress system reactivity without sufficient recovery can lead to permanent changes in normal cardiovascular functioning (McEwen, 1998). As a result of a poor work environment and insufficient possibilities for coping, psychophysiological recovery becomes insufficient. According to the insufficient recovery theory, compromised recovery disturbs physiological processes, like sympathetic nervous system activity and hormone secretion, and, eventually, leads to psychological and physical health problems. (Kompier & Taris, 2004.)

However, workload and recovery in shift work has been sparsely studied in relation to the work stress models. Recovery from work is particularly important when recovery opportunities during work time are insufficient (Geurts & Sonnentag, 2006). Lack of recovery may be a greater health problem than the strain itself (Lundberg, 2005). When recovery is incomplete and the employee is, for example, still tired from the previous work period, she has to expend extra effort to perform properly at work (Pennonen, 2011). Females are particularly at risk of insufficient recovery, as their stress levels stay elevated after work more often than males (Lundberg & Frankenhaeuser, 1999).

Incomplete recovery is presented as an explanatory mechanism underlying the relationship between acute stress reactions and chronic health impairment (Geurts & Sonnentag, 2006) (Figure 3). When recovery from shift work is considered, a model should include, for example, irregular working hours and individual factors (Lindholm, 2013). Figure 4 presents the author's construction of a recovery model in shift work. Recovery can be promoted by introducing sleep-promoting principles into the shift rotation (Härmä, 2006), as chapter 2.2.2 Favourable shift schedules recommends.

## 4 REVIEW OF THE LITERATURE ON STRESS...

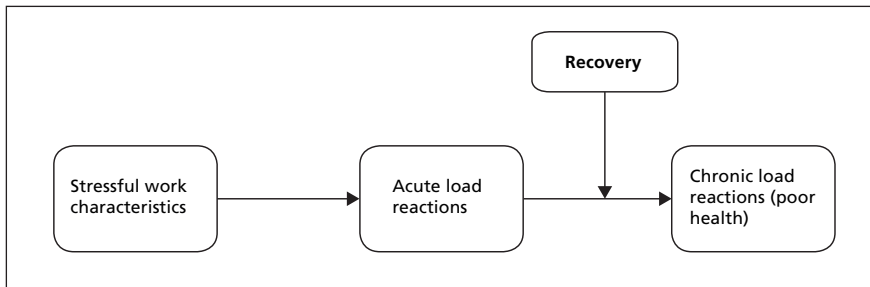


Figure 3. Model of work, recovery and health (Geurts & Sonnentag, 2006).

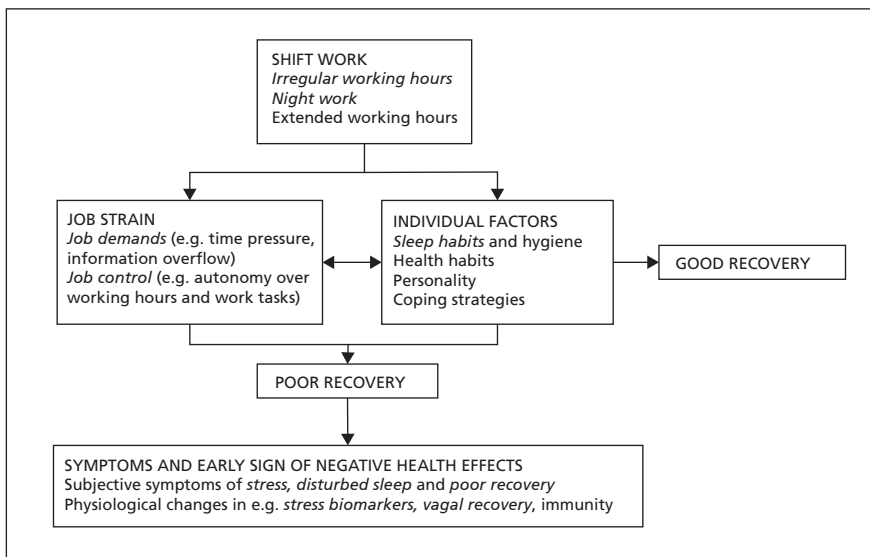


Figure 4. Model of shift work, job strain, sleep and early signs of negative health effects. Concept in *italics* refer to the objects of this study.

## **5 SUMMARY OF THE STATE OF THE EVIDENCE**

Most of the job strain studies are cross-sectional and have subjective measures of job strain (Ayas et al., 2003; Kalimo et al., 2000; Ohlin et al., 2007), which allows for subjectivity bias (i.e. bias from differences in individual reactivity and response styles) to affect the results (Rugulies, 2012). Previous studies on job strain have also been mainly conducted among daytime workers (Kompier et al., 2012). In addition, relatively little research is available on work-related stress and sleep (Åkerstedt, 2006), when sleep is measured not merely with subjective methods.

The long-term effects of shift work on sleep are rather poorly understood (Åkerstedt & Wright, 2009). It appears there are no previous studies that have measured both exposure to job strain and sleep quantity with actigraphy in shift work. Previous studies reporting shift-specific sleep lengths have been conducted among male, or predominantly male, samples (Bonnefond et al., 2006; Lützhöft et al., 2010; Paterson et al., 2012; Saksvik et al., 2011). Despite extensive research among nursing staff, there are few earlier studies reporting shift-specific sleep lengths and/or sleep disturbances according to job strain. A few field studies have explored how work stress links to shift-specific workload, sleepiness and recovery among shift workers. It is not known whether extended sleep after the night shift or during days off compensate for the prior sleep loss (Åkerstedt & Wright, 2009).

Stress reaction is a multifaceted phenomenon and requires a multidimensional measurement approach (Nater & Rohleder, 2009), but studies with multiple physiological measurements including, for example, salivary alpha-amylase are sparse. Overall, there are only a few earlier publications on work stress and sAA (Groer et al., 2010; Limm et al.,

2011; Wingenfeld et al., 2010; Wong et al., 2012) and among shift workers, results of both normal (Wingenfeld et al., 2010) and flatter (Wong et al., 2012) diurnal slopes have been observed. The studies of cortisol profiles during stress show conflicting results (Miller et al., 2007; Wong et al., 2012). Only a limited number of studies have examined the association between heart rate variability and work-related stress (Clays et al., 2011). The literature on the effects of work-related factors on HRV is predominantly based on cross-sectional studies that have found both alterations and no alterations in HRV (Togo & Takahashi, 2009). Moreover, I am not aware of either earlier studies on TSST solely among health care staff or earlier studies that have combined a laboratory measure of stress reactivity with field measurements of stress biomarkers. It is important to study stress in both laboratory and field because the laboratory stress tests are assumed to reflect the way individuals react in real life (Kidd et al., 2014).

To address some of the limitations in the existing evidence, this study aims to extend the previous knowledge on job strain and shift work with multiple behavioural and psychophysiological measurements. Aggregated, ward-level job strain groups used in this study is a new way to approach job strain and reduce subjectivity bias. Only limited information exists on shift-specific sleep and recovery, especially in females. There is a limited number of earlier publications on job strain and psychophysiological workload and recovery, measured with, for example, heart rate variability and salivary alpha-amylase. Moreover, there are no earlier studies that have combined laboratory measures of stress reactivity with field measurements of stress biomarkers in the same individuals. The present study will address these limitations.

## **6 AIMS OF THE STUDY**

The overarching aim of this study was to determine the association of long-term exposure to stressful work environment with sleep, and psychophysiological recovery among female night shift workers. This thesis is based on four studies. The objective and hypotheses are as follows:

1. To study the association of job strain with sleep and alertness among shift working health professionals.

The main hypothesis was that impaired sleep is prevalent in shift workers. Among them, high job strain is associated with greater impairment of sleep quantity and quality. This has the effect of decreasing duty alertness more than a low job strain.

2. To study the extent to which job strain is explained by working hours, shift arrangements, perceived workload and recovery.

The study hypotheses were that high job strain is associated with extended working hours and non-ergonomic shift scheduling as well as higher perceived workload and higher need for inter-shift recovery than low job strain.

3. To study, in field conditions, the association of shift workers' high job strain with vagal recovery during sleep after a shift.

The main hypothesis was that high job strain impairs vagal recovery from a previous work shift and is manifested as a higher heart rate and lower heart rate variability during sleep than in employees with low job strain.

## 6 AIMS OF THE STUDY

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4. To study the association of job strain with biomarkers of stress in both laboratory and field conditions.

The study hypotheses were that a high job strain is associated with augmented acute salivary cortisol and alpha-amylase responses both in the laboratory and in field conditions, with blunted cortisol awakening response, elevated cortisol evening levels, and decreased total salivary alpha-amylase secretion.

## **7 METHODS**

### **7.1 Study design and participants**

The participants were recruited from “The Finnish Public Sector Study” (FPSS) survey in 2008 (n=52 891, response rate 72%). Native Finnish-speaking female health care professionals, who worked night shifts were identified (n=5 615) from this sample. (Figure 5.) The sample included five hospitals or health care districts and four cities in southern Finland. In the different health care organizations, the data collection took place between June 2009 and January 2011. The participants were from 59 wards which had an average of 37 employees.



## 7 METHODS

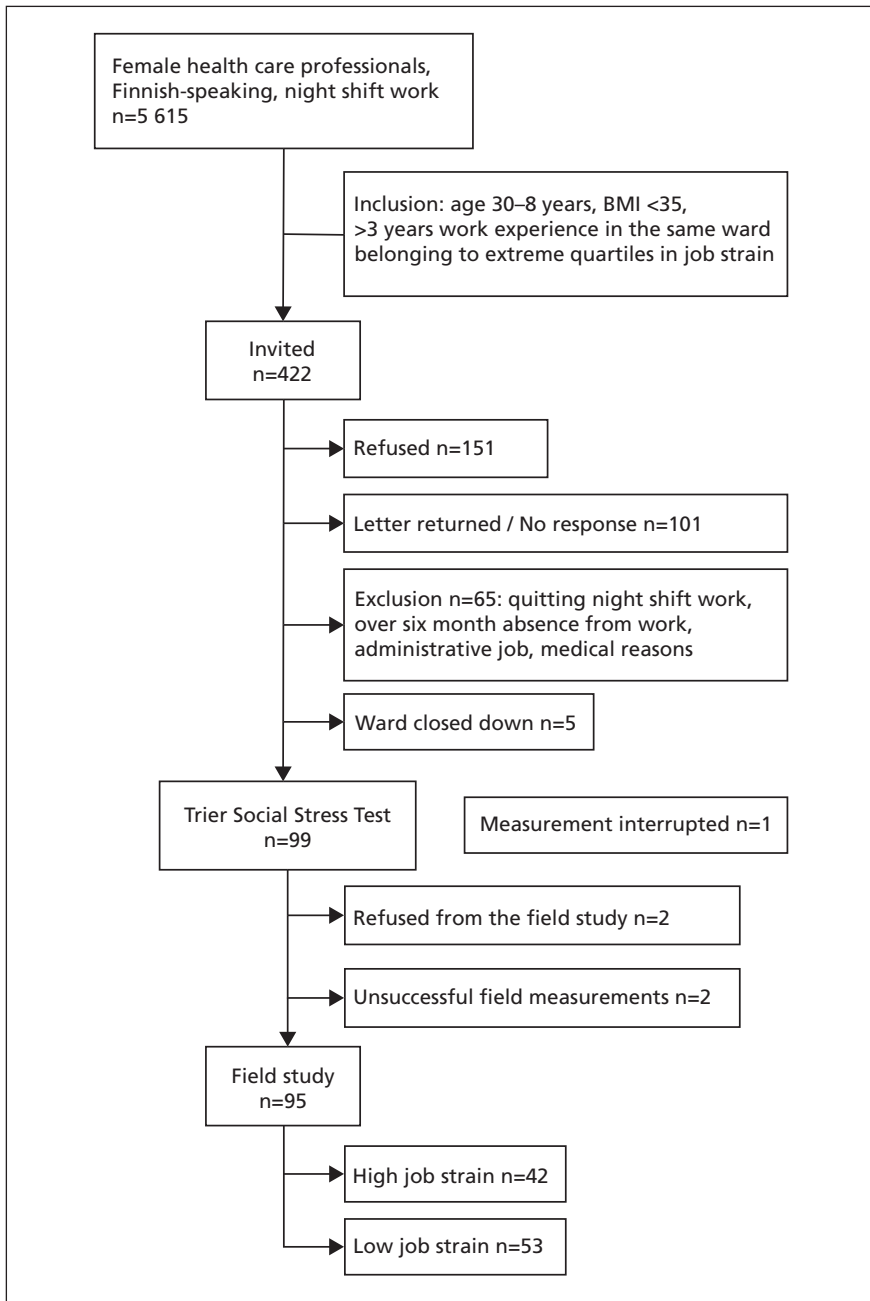


Figure 5. Flow chart of the study.

## 7 METHODS

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Job strain was determined by Karasek's Job Content Questionnaire (JCQ) in Finnish (Kouvonen et al., 2005), with three questions on "job demand" (JD) and nine questions on "job control" (JC) (Table 4) using a 5 -point Likert -type scale ranging from 1 (strongly disagree) to 5 (strongly agree). The high (HJS) and low job strain (LJS) groups were divided by grouping the wards with at least 5 respondents to the JD and JC scales on the same ward, using median split to identify HJS (high demands and low control) and LJS (low demands and high control). With these cut-points, it was possible to identify employees from these wards who belonged to the HJS or the LJS groups based on their individual mean scores of JD and JC.

**Table 4. The Job Content Questionnaire items for job demands (1–3) and job control (4–12).**

- 
1. I have to work very hard.
  2. My job involves an excessive amount of work.
  3. I don't have enough time to get my work done.
  4. My job allows me to make a lot of decisions on my own.
  5. My job requires me to be creative.
  6. My job requires that I learn new things.
  7. My job involves a lot of repetitive work.
  8. I have a lot of say what happens on my job.
  9. My job requires a high level of skill.
  10. I get to do a variety of different things on my job.
  11. I have an opportunity to develop my own special abilities.
  12. On my job, I have very little freedom to decide how I do my work.
- 

To increase the contrast between job strain groups, the employees belonging to the quartile with least strain in the HJS group (n=86) and most strain in the LJS group (n=48) were excluded (Figure 6). The reliabilities for JCQ for the whole public sector sample (n=52 891) were good (Cronbach's  $\alpha=0.77$  for JD and  $\alpha=0.82$  for JC, items 7 and 12 were reversed when computed).

## 7 METHODS

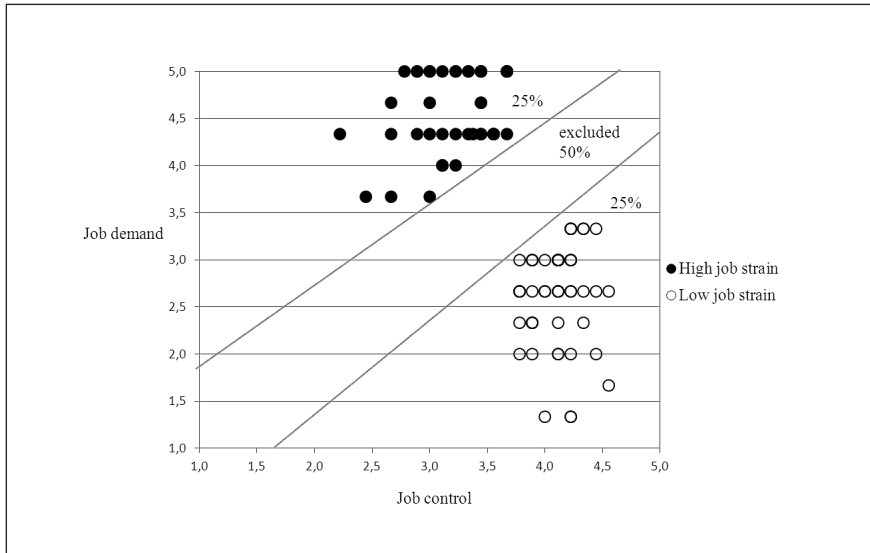


Figure 6. Participants positions on the Job Demand and Job Control scales (1=low, 5=high).

A letter of invitation was sent to the workplace of each employee, fulfilling inclusion criteria ( $n=422$ ). These criteria were: shift work including at least one night shift per three weeks, age between 30 and 58 years, native Finnish speaker, Body Mass Index (BMI) under 35, at least three years' work experience in the same ward, and less than 6-months absenteeism from work (for example, maternity leave) during the past three years. Age limits were set to ensure exposure to working life and to minimize the proportion of retiring. An upper limit for BMI was used to minimize the probability of participants with non-diagnosed sleep apnea (Bixler et al., 2001) as the participants were not screened for sleep disorders. Volunteers with a disease or medication affecting cognitive functions, coronary heart disease, insulin-treated diabetes mellitus, as well as pregnant or breast feeding mothers, were excluded. The main reasons for exclusion ( $n=65$ ) were changing ward or workplace after the 2008 FPSS survey ( $n=22$ ) or ceasing night shift work ( $n=21$ ).

The representativeness of the sample of 95 actual participants was tested by comparing them to the 422 invited participants. There were

no statistical differences ( $p$ -values  $>0.11$ ) between participated and invited on age, level of education<sup>1</sup>, work experience, number of children, BMI, habitual sleep length, sleep need, or sleep disturbances. There were more participants from the low strain group than the high strain group ( $p<0.01$ ) and fewer from the two major health care districts ( $p=0.00$ ). The participants were more often from medical-surgical wards than other wards (for example, intensive care, emergency or maternity units) compared to those invited to participate (45 vs. 33%,  $p<0.04$ ).

### 7.2 Ethics

The study protocol was approved by the Coordinating Ethical Committee of the Hospital District of Helsinki and Uusimaa. All the study participants were volunteers and written informed consent was obtained from each participant. The participants were reimbursed for travelling expenses for the required laboratory visits to the Finnish Institute of Occupational Health (FIOH, Helsinki, Finland) with fares on public transportation and a 50-Euro compensatory allowance for participation.

### 7.3 Measurements

#### 7.3.1 Questionnaires

The study included an internet questionnaire featuring background variables. The background variables used in this study were age, level of education, shift work experience, physical activity (times per week, at least 30 min/day, during the past three months), number of children, smoking habit, alcohol consumption, medication use, stressful life events during the past 12 months (Dohrenwend et al., 1978), morningness-eveningness questionnaire (MEQ) (Smith, Reilly, & Midkiff, 1989), Beck's Depression Inventory (BDI-II) (Beck, Steer, & Brown, 1996), sleep duration and frequency (never/seldom, quite seldom, quite often

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<sup>1</sup> In Finland, to graduate as a nurse you must complete a three and a half-year (210 ECT credits) bachelor's degree after either high school or the nursing assistants' degree. A nursing assistant's degree is a three-year course after comprehensive school.

or often/frequently) of sleep disturbances (difficulties initiating sleep, difficulties re-initiating sleep after waking up, excessive daytime sleepiness or occurrence of any sleep complaint several times a week) during the past four weeks and Epworth Sleepiness Scale (ESS), where the cut-point for sleepiness was set at 10 (scale 0–24) (Johns, 1991). There was no missing data in the questionnaire because an answer was required for every question.

### 7.3.2 Three week field measurements

An overview of the three week field measurements that are presented in the following chapters is illustrated in Figure 7.

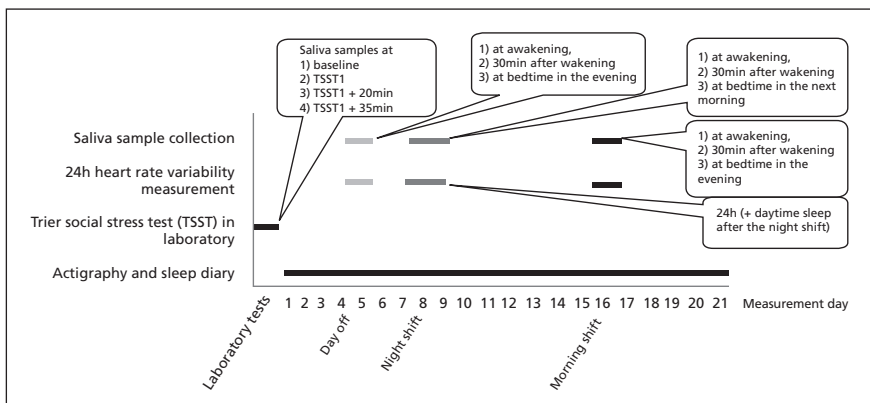


Figure 7. An example of the schedule of the field measurements.

### Actigraphy

Actigraphy has been used to study sleep/wake patterns for more than 30 years (Ancoli-Israel et al., 2003) and it has been found to be a reliable and valid measure of sleep in a healthy adult populations (Littner et al., 2003). In this study (Studies I–IV) actigraphy was used to analyse the sleep-wake rhythm for three weeks. The participants wore the actigraphy device (Actiwatch AW7, Cambridge Neurotechnology, Cambs, UK) (Figure 8) on their non-dominant wrist continuously, except for moments of hygiene concern at the workplace.



Figure 8. The actigraphy device.

Actigraphy data was collected using 0.25 minute epochs and scored using 1 minute epochs. Sleep periods were calculated from sleep onset to sleep offset. Start and end times for sleep periods were corroborated with data recorded in the sleep diary. Sleep efficiency (SE) was calculated from the ratio of time asleep to the time in bed. The limit of reduced SE was set to be  $<85\%$  (Astill et al., 2013). Sleep latency was calculated with a 3-minute immobility rule. The upper limit for a normal sleep latency was set to  $\leq 20$  minutes, which is in concordance with duration of the Multiple Sleep Latency Test (Littner et al., 2005).

### **Sleep diary**

In a sleep diary, the participants kept a record of times at which they went to sleep and got up, and their working hours. The participants evaluated their alertness using the Karolinska Sleepiness Scale (KSS) (Åkerstedt & Gillberg, 1990) before and after every work shift. The KSS is a standard measure of sleepiness in occupational studies of performance and has demonstrated validity with electroencephalography (EEG) (Torsvall et al., 1989). Severe sleepiness was defined as a KSS score of  $\geq 7$  (Åkerstedt & Gillberg, 1990), because physiological intrusions of sleep in EEG or EOG usually start at score of 7 (Åkerstedt & Wright, 2009).

Mental and physical workloads were evaluated in each work shift using a five-point Likert scale, ranging from much too low to much too high. Feelings of relaxedness before going to sleep were scored with a

## 7 METHODS

9-point Likert scale, ranging from extremely relaxed to extremely nervous. Recovery from previous work shift was evaluated after waking up from recovery sleep using a five-point Likert scale, the range being from complete recovery to no recovery at all. Sleep latency, being awake during the night, ease of waking up, and number of and duration of naps were also scored. The duration of naps was scored with a 15-minute accuracy. The participants also reported the amount of alcohol or caffeinated drinks and use of sleep promoting medication during the measurements. The sleep diaries were completed with 95% of values. The sleep diary results are reported in Studies I and II.

### 7.3.3 The three pre-selected field measurement days

The three pre-selected measures were made on three non-consecutive days (24h) with one morning shift (mostly from 07:00 to 15:00), one night shift (mostly from 21:00 to 07:00) and one day off (Figure 9 showing also the selected sleep periods for heart rate variability analysis).

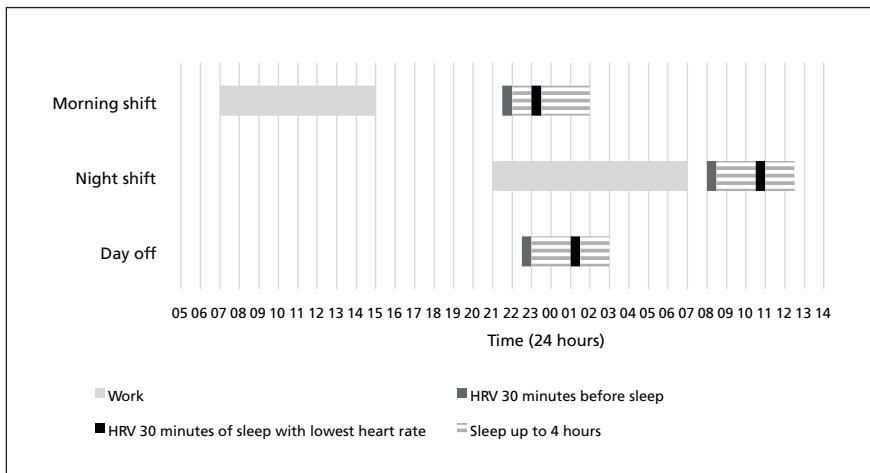


Figure 9. The average timing of work shifts, sleep and HRV measurement periods during the pre-selected measurement days.

## 7 METHODS

To standardize the effect of previous work shifts and circadian rhythm disruption, the pre-selected measurement days were planned as follows: (i) the morning shift was at least the third consecutive morning shift, where the effect of several early awakenings was demonstrated, (ii) the night shift was the first shift after a morning or evening shift, where the change of sleep-wake cycle rhythm was most evident and (iii) the day off was the second consecutive day off, where the circadian rhythm would be close to the participants' normal rhythm. Table 5 presents an example of a typical three week roster including the field measurement days.

**Table 5. An example of a typical three week roster including the three pre-selected field measurement days. M = morning shift, E = evening shift, N = night shift, - = day-off.**

	Shift type	Start time	End time
Mon	M	07:00	15:00
Tue	E	14:00	21:30
Wed	A	07:00	15:00
Thu	-	-	-
<b>Fri<sup>1</sup></b>	-	-	-
Sat	E	14:00	21:30
Sun	M	07:00	15:00
<b>Mon<sup>2</sup></b>	<b>N</b>	<b>21:00</b>	<b>24:00</b>
Tue		00:00	07:15
	N	21:00	24:00
Wed		00:00	07:15
Thu	-	-	-
Fri	-	-	-
Sat	E	14:00	21:30
Sun	M	07:00	15:00
Mon	M	07:00	14:15
<b>Tue<sup>3</sup></b>	<b>M</b>	<b>07:00</b>	<b>16:00</b>
Wed	-	-	-
Thu	-	-	-
Fri	E	14:00	21:30
Sat	M	07:00	15:00
Sun	M	07:00	15:00

<sup>1</sup> second consecutive day off

<sup>2</sup> first night shift after morning/evening shift

<sup>3</sup> third consecutive morning shift



### **Psychomotor vigilance test**

A 5-minute version of PVT (Psychomotor Vigilance Test) (Wilkinson & Houghton, 1982) was used in this field study (Study I) for practical reasons. Instead of a standard 10-minute test, a 5-minute version is practical and viable in field conditions (Loh et al., 2004). The PVT was installed on HP ipaq 514 mobile phones (Hewlett-Packard, Hewlett-Packard Company, Palo Alto, California, USA), where the SIM-card had been removed. Answering was done by pressing the zero button. Three of the mobile phones were mistakenly set up with a 10 minute test and 6 participants did a longer version of the test before setting up was redone. Their data was analysed using the first 5 minutes of the PVT.

The PVTs were carried out (i) in the morning shift between 12–15 pm at work and in the evening between 19–21 pm at home, (ii) before the night shift between 19–21 pm at home and between 02–04 am at work and (iii) on the day off between 12–15 pm. To minimize the effect of learning, the participants were instructed to practise the PVT three times before the first test day (Dinges et al., 1997). Reaction times >500 milliseconds were regarded as lapses. PVT tests were completed in 97% of the planned tests.

### **Heart rate variability**

In this study (Study III) a 24-hour interbeat interval (IBI). Data was collected using the Firstbeat Bodyguard 1.1 device (Mega Electronics Ltd, Kuopio, Finland). The electrodes were placed in the V2 and V5 electrode positions in the standard 12 lead ECG system and the ground electrode below the right clavicle (collar bone) (Figure 10). The participants were instructed to continue their normal way of life, but to refrain from heavy exercise during the 24 hour measurement period and to replace the electrodes after a shower or sauna.

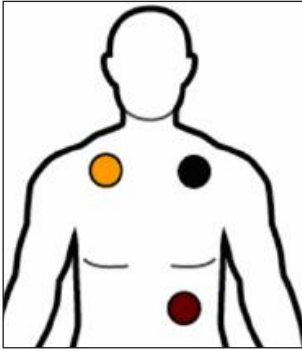


Figure 10. Electrode placements in the heart rate variability measurement. (Firstbeat Technologies Oy.)

The HRV data was analysed using Matlab, using a custom code and a code based on Biosignals (Niskanen et al., 2004). The raw IBI series was screened for artifacts using a method presented by Xu and Schuckers (2001). In this method, each IBI is compared with the median of the 25 surrounding IBIs and the last accepted IBI. The current interval is termed an artifact if it differs more than 20% from both the median and the previous accepted interval. No correction of artifacts were attempted, and IBIs marked as artifactual were deleted, as were IBIs corresponding to an instantaneous heart rate outside the range 30 to 190 beats per minute (bpm) (Wong et al., 2012). The power spectrum was evaluated using the Lomb-Scargle periodiogram, allowing direct spectral analysis of unevenly sampled signals.

The minimum requirement of inclusion of data in the HRV analyses was at least 4 hours of sleep following the shift to gather slow-wave sleep and metabolically most restorative sleep (Lindholm et al., 2012; Stein & Pu, 2012). The time-domain metrics included in the analysis were RMSSD (the square root of the squared mean of the differences between successive IBIs) and average heart rate (HR). The frequency domain metrics were low frequency power (LF), high frequency power (HF) and the LF-to-HF power ratio (LF/HF). The HRV analyses were performed in 120 second segments with 50% overlap. Only segments with at least 64 IBIs were analysed to ensure sufficient data. The period

of lowest heart rate was defined as the 30-minute segment within the first four hours of sleep during which the mean HR was the lowest (Figure 9). The mean of the values from all 5-minute segments was calculated and this value was used in the subsequent statistical analyses.

At least four hours of successful sleep-time heart rate variability data was obtained from 91% (n=86) of the participants measured on the morning shifts, and 90% (n=85) of the participants measured on the night shifts and 88% (n=84) of participants measured on their day off. The heart rate variability results are reported in Study III.

### **Salivary cortisol and alpha-amylase**

In Study IV, on the pre-selected measurements days, the participants were instructed to collect saliva sample and record the exact time it was collected, i) immediately after waking up (AW), ii) 30 minutes after waking up (AW30) and iii) in the evening before brushing their teeth and going to sleep, preferably around 10 pm or after a night shift, or in the morning before going to sleep, preferably around 8 am (Figure 7). The saliva samples were collected with Salivette tubes and cotton rolls, which the participant chewed for one minute and then placed in the Salivette tube. Participants were instructed to refrain from eating, drinking and heavy exercise before collection of the saliva samples.

The times for saliva sample collection during the morning shift were on average at 05:27 (AW), 05:57 (AW30); on the evening at 22:36; on the night shift at 08:08 (AW), 08:41 (AW30) and 08:06 next morning before going to sleep; in the evening and during the day off at 07:56 (AW), 08:21 (AW30) and 21:34. On the morning shift, the AW and AW30 were collected on average 6 and 30 minutes after the end of sleep. On the night shift the samples were collected 8 and 38 minutes after the end of sleep. On the day off, the samples were collected 6 and 30 minutes after the end of sleep.

The samples were stored in home refrigerators and sent to FIOH by regular post on the following weekday, as these samples have good tolerance to the temperatures prevailing during shipment (Andrews, Ali & Pruessner, 2013; Clements & Parker, 1998; Rohleder & Nater, 2009). The samples were analysed as described in the test protocol of the Trier Social Stress Test (chapter 7.3.4 Laboratory study: The Trier Social Stress

Test). Salivary cortisol awakening response was considered to be within the range of normal values, when the AW30 sample was 50–60% larger than the AW sample (Chandola et al., 2010). Salivary cortisol evening levels were considered elevated at levels above 3 nmol/l with ELISA (enzyme-linked immunosorbant assay), which is comparable to 5 nmol/l in mass spectrometer (The Association for Clinical Biochemistry and Laboratory Medicine, 2014).

### **7.3.4 Laboratory study: the Trier Social Stress Test**

In Study IV, the Trier Social Stress Test (Kirschbaum et al., 1993) was conducted in FIOH at approximately 13:00 pm. The test included four saliva samples of cortisol and alpha-amylase, a 10-minute anticipation period and a 10-minute test period that consisted of speech and performing mental arithmetic. The first saliva sample (baseline) was collected after a rest period after arriving at FIOH at around 10:30 am. The TSST saliva samples were collected at the beginning and end of the TSST and 15 minutes after completing the test.

In the beginning of the TSST, the TSST1 a saliva sample was collected. A research nurse directed the participant to room B and explained the tasks she would subsequently perform. The participant was told to take on the role of a job applicant invited to a personal interview for a nurses' job by preparing a 5-minute free speech. She was given 5 minutes to prepare the speech. The participant was told to stand at a microphone facing a video camera and a staff manager. It was announced that a voice frequency analysis, as well as an analysis of nonverbal behaviour and an analysis of the participant's performance would be conducted afterwards. The participant was told to convince the staff manager in the 5-minute presentation that she was the best applicant for the position. After the preparation the participant was guided to room A, where one person she had not met before was sitting at a table, behaving neutrally. The participant gave the speech and whenever finishing the speech in less than 5 minutes, she was asked to continue in a standardized way as described in the TSST protocol (Kirschbaum et al., 1993).

After 5 minutes, the staff manager asked the participant to serially subtract the number 13 from 2083 as fast and as accurately as possible. On every failure the participant had to start again from 2083. After

10 minutes precisely the mental arithmetic task was stopped and the TSST2 saliva sample was collected. The research nurse informed the participant about the goal of the study and that no video analysis would be performed. The TSST3 saliva sample was collected 15 minutes after finishing the TSST. Neither the research nurse nor the staff manager was aware of which job strain group the participant belonged to.

The saliva samples were analysed in the FIOH laboratories (Helsinki, Finland). Values of salivary cortisol were analysed using a LIA kit (LIA, IBL, Hamburg, Germany) and the measurement range was 0.43–110 nmol/l. Salivary AA was analysed with Salivary  $\alpha$ -amylase Kinetic enzyme assay kit (item No 1-1902, Salimetrics, USA). Samples between 2.0 and 900 U/mL were accepted (Wong et al., 2012). Samples that exceeded 400 U/ml (linearity limit) were rerun using a diluted concentration. The collection and analysis of the saliva samples were successful in 99% of samples for both cortisol and alpha-amylase.

### 7.4 Statistical methods

Statistical analyses were conducted by SPSS 17.0, PASW 18.0 (Chicago, IL, USA) and R (R Core Team, 2013). In all the studies I–IV, the comparisons of the discrete characteristics of the study groups were performed using the Pearson's Chi-square ( $\chi^2$ )-test and comparisons for continuous variables were done using independent samples t-test and one-way analysis of variance (ANOVA). The Pearson's  $\chi^2$  test was used to compare group differences in job strain and educational level. One-way analysis of variance (ANOVA) was used to explore age differences between the study groups. There was a statistically significant group difference in level of education, which was used as a covariate. Physical activity was not regarded as a confounding factor but as a possible mediator of an effect due to earlier results that job strain may increase physical inactivity (Fransson et al., 2012a). In all the analyses, p-values <0.05 were considered statistically significant.

In Study I, job strain group differences in sleep length and efficiency were tested with the Mann-Whitney U-test or Fisher's exact test. Possible group differences in sleep disturbances and napping were tested with Pearson's  $\chi^2$ -test, independent samples t-test and the Mann-Whitney

U-test. PVT results were analysed with the Mann-Whitney U-test, independent samples t-test and one-way analysis of variance (ANOVA).

In Study II, job strain group differences in working hours and number and duration of work shifts were tested with independent samples t-test, the Mann-Whitney U-test and the Pearson's  $\chi^2$ -test. Evaluations of workload, sleepiness and recovery were tested against group differences using the Pearson's  $\chi^2$ -test, logistic regression analysis and independent samples t-test.

In Study III, the heart rate variability parameters (HR, HF, LF, LF/HF ratio, RMSSD) were calculated with R packages using the packages ggplot2 (Wickham, 2009), multtest (Pollard et al.) and boot (Canty & Ripley, 2013; Davison & Hinkley, 1997). The bootstrapping is well suited for samples of limited size and also allows confidence intervals to be estimated for the parameters of interest. The CIs enable the study of the stability of the individual measures and allow parameters to be compared between groups. The effect of job strain group and shift type (morning shift, night shift or day off) on the HRV metrics was compared using Wilcoxon's Signed Rank Test, with p-values adjusted for multiple testing using the Westfall & Young resampling-based step-down minP adjustment method (Westfall & Young, 1993). The 95% confidence intervals were estimated using the bias-corrected and accelerated (BCa) bootstrap method (Efron, 1987).

In Study IV, a logarithmic transformation of the original values was used because the distributions for the salivary biomarkers were mostly skewed. The total secretion of salivary cortisol and salivary alpha-amylase was calculated with the formula for area under the curve with respect to ground ( $AUC_g$ , nmol/l x minutes) (Pruessner et al., 2003), with an assumption of linearity between consecutive points. The General linear model (GLM) ANOVA for repeated measures was used to test profiles of the biomarkers of stress. The sAA over cortisol ratios were calculated from the  $AUC_g$  results (Ali & Pruessner, 2012).

## **8 RESULTS**

### **8.1 Descriptive characteristics**

Of the 95 participants, 42 (44%) belonged to the high job strain group and 53 (56%) to the low job strain group. The participants worked most often in medical-surgical wards (45%, n=43) and intensive care or emergency units (15%, n=14). Their mean age was 47 years (range 31–59), with no difference between the job strain groups. (Table 6.)

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**Table 6. The descriptive statistics of study participants.**

	High Job Strain n=42		Low Job Strain n=53		Df	T-value	P-value
	Mean	(SD)	Mean	(SD)			
Age (years)	47.7	(6.4)	46.7	(7.5)	93	0.64	0.52 <sup>1</sup>
BMI <sup>2</sup> (kg/m <sup>2</sup> )	26.7	(4.1)	25.6	(4.0)	93	1.29	0.20 <sup>1</sup>
Shift work experience (years)	18.7	(7.9)	16.9	(7.6)	90	1.11	0.27 <sup>1</sup>
BDI-II score <sup>3</sup>	7.5	(6.1)	5.3	(4.3)	-	-	0.13 <sup>4</sup>
	%	(n)	%	(n)	$\chi^2$ value		P-value
Education					5.38		0.02 <sup>5</sup>
Nurse <sup>6</sup>	60	(25)	81	(43)			
Nursing assistant <sup>7</sup>	40	(17)	19	(10)			
Physical activity <sup>8</sup>					9.25		<0.01 <sup>9</sup>
<3 times a week	29	(12)	6	(3)			
≥3 times a week	71	(30)	94	(50)			
Family care-giving responsibility <sup>10</sup>					0.44		0.51 <sup>5</sup>
Yes	62	(21)	69	(31)			
No	38	(13)	31	(14)			
Stressful life event <sup>11</sup>					0.93		0.34 <sup>5</sup>
Yes	66	(27)	75	(39)			
No	34	(14)	25	(13)			
Chronotype <sup>12</sup>					0.31		0.58 <sup>5</sup>
Morning-type	45	(19)	51	(27)			
Evening-type	55	(23)	49	(26)			

<sup>1</sup> independent samples T-test

<sup>2</sup> body Mass Index, normal weight <25

<sup>3</sup> Beck's Depression Inventory -II

<sup>4</sup> Mann-Whitney U-test

<sup>5</sup> Pearson Chi-Square

<sup>6</sup> nurse, midwife, public health nurse, X-ray nurse, deaconess nurse

<sup>7</sup> nursing assistant, practical nurse, nursery nurse, mental nurse

<sup>8</sup> at least 30 min/day, during past three months

<sup>9</sup> Fischer's exact test

<sup>10</sup> children under 18 years

<sup>11</sup> during the past year

<sup>12</sup> Morningness-eveningness questionnaire



No differences between the two job strain groups were found when comparing average shift work experience, family care-giving responsibilities, stressful life events or chronotypes (Table 6). The participant groups showed no differences in life-style factors (current smoker HJS & LJS 19%,  $p>0.98$  and regular alcohol consumption HJS 53%, LJS 55%,  $p>0.85$ ), medication use and measurement season (data not shown). Two of the participants in the HJS group scored points typical for clinical depression compared to none in the LJS group ( $p<0.11$ ). The proportion of nurses was higher in the LJS group (81%) than in the HJS group (60%,  $p=0.02$ ) and the LJS group reported higher physical activity than the HJS group ( $p<0.01$ ).

### **8.2 Work shifts and working hours**

The work shift data consisted of a total of 1 186 shifts. The number of realized total working hours during the three week measurement period (HJS 109:55h, LJS 113:15h,  $p=0.30$ ) showed no job strain group differences when full-time employees ( $n=89$ ) were included. The HJS group had, on average, one morning shift more and, conversely, one extended shift less than the LJS group ( $p=0.01$ ;  $p=0.02$ ). All participants ( $n=6$ ) who experienced quick returns ( $<9$ h) were in the HJS group ( $p<0.01$ ). Single days off from work were more common in the HJS group (19% of all days off) than in the LJS group (10%,  $p<0.01$ ). (Table 7.) The majority (59%,  $n=160$  shifts) of evening shifts were followed with a quick return to a morning shift with an average shift interval of 9:56 hours (SD 0:47h).

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**Table 7. Average number of different work shifts and days off per three weeks.**

	High Job Strain		Low Job Strain		Df	T-value	P-value
	Mean	(SD)	Mean	(SD)			
During three weeks							
All work shifts	12.7	(1.9)	12.3	(1.8)	93	0.96	0.34 <sup>1</sup>
Morning shifts	7.0	(1.9)	5.8	(2.3)	93	2.72	<0.01 <sup>1</sup>
Evening shifts	2.9	(1.4)	2.8	(1.7)	93	0.98	0.64 <sup>1</sup>
Night shifts	2.4	(1.4)	2.6	(1.5)	93	-0.52	0.61 <sup>1</sup>
Extended shifts <sup>2</sup>	0.4	(0.6)	1.2	(2.0)	-	-	0.02 <sup>4</sup>
Quick returns <sup>3</sup> <9h	0.2	(0.6)	0	(0)	-	-	<0.01 <sup>4</sup>
All quick returns	1.9	(1.2)	1.5	(1.0)	93	1.80	0.07 <sup>1</sup>
Days off on weekdays	4.2	(1.6)	4.5	(1.8)	93	-0.82	0.41 <sup>1</sup>
Days off on weekends <sup>5</sup>	2.5	(1.3)	2.6	(1.6)	93	-0.39	0.70 <sup>1</sup>
	<b>%</b>	<b>(n)</b>	<b>%</b>	<b>(n)</b>	<b>χ<sup>2</sup> value</b>		<b>P-value<sup>6</sup></b>
Single work shifts <sup>7</sup>	7	(3)	9	(5)	0.16		0.69
Single days off <sup>7</sup>	79	(33)	49	(26)	8.67		<0.01

<sup>1</sup> independent samples T-test

<sup>2</sup> morning shift and evening shift

<sup>3</sup> morning shift(s) after an evening shift(s) (n=84; HJS n=37, LJS n=47)

<sup>4</sup> Mann-Whitney U-test

<sup>5</sup> including public holidays

<sup>6</sup> Pearson Chi-Square

<sup>7</sup> at least once in three-week measurement period

The average duration of morning and evening shifts was approximately eight hours and showed no job strain group differences. The HJS group night shifts started on average later but were shorter than in the LJS group (at 20:57 vs. 20:40,  $p<0.04$ ; 10:26h vs. 10:51h,  $p<0.01$  respectively). The proportion of participants that worked extended shifts was 39% (n=37,  $p<0.10$  for group difference). The proportion of extended shifts (>12h) (Table 8) and consecutive extended shifts (HJS 2% vs. LJS 13%,  $p\leq 0.06$ ) from all work shifts was higher in the LJS group than in the HJS group, but these differences were not statistically significant.

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**Table 8. Average duration (hours) of work shifts per three weeks and proportions of normal and extended work shifts.**

	High Job Strain		Low Job Strain		Df	T-value	P-value
	Mean	(SD)	Mean	(SD)			
During three weeks							
Average shift duration							
Morning shifts	8:01	(00:14)	8:02	(00:31)	91	-0.18	0.91 <sup>1</sup>
Evening shifts	7:48	(00:37)	7:50	(00:28)	84	-0.28	0.78 <sup>1</sup>
Night shifts	10:26	(00:23)	10:51	(00:40)	93	-3.63	0.01 <sup>1</sup>
Extended shifts <sup>2</sup>	13:23	(01:18)	13:14	(00:57)	35	0.43	0.67 <sup>1</sup>
Proportions of shift durations	%	(n)	%	(n)	Df	T-value	P-value
Short (<8h)	59	(42)	49	(53)	93	2.06	0.04 <sup>1</sup>
Normal (8-12h)	37	(42)	36	(53)	93	0.21	0.84 <sup>1</sup>
Extended (>12h)	3	(42)	14	(53)	-	-	0.06 <sup>3</sup>

<sup>1</sup> independent samples T-test

<sup>2</sup> morning shift and evening shift

<sup>3</sup> Mann-Whitney U-test

The employees' own wishes in shift planning were more often taken into account in the LJS group (89 vs. 67%,  $p=0.01$ ). The HJS group felt that they were less frequently able to have an effect on the possible solutions concerning problems in their shift planning (19 vs. 41%,  $p=0.01$ ).

### 8.3 Sleep

#### 8.3.1 Sleep length and quality

The actigraphy data showed that the main sleep period lasted, on average, 06:46 hours in the HJS group and 06:51 hours in the LJS group (Table 9), with no statistically significant group difference. The shortest sleep durations were recorded after night shifts in both job strain groups. The LJS group slept on average 28 minutes longer than the HJS group, both

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after evening shifts and quick returns, but these group differences did not reach statistical significance ( $p=0.06$  and  $0.08$ , respectively). After the pre-selected morning shift, sleep duration was on average shorter in the HJS group than LJS group for those who were about to continue with another morning shift the next day (6:18 vs. 7:32h,  $p<0.03$ ).

Sleep efficiency (SE) was more often reduced ( $\leq 85\%$ ) before morning shifts in the HJS group than in the LJS group (21 vs. 6%,  $p=0.02$ ) but not on average or in connection with other work shifts, quick returns (Table 9) or the pre-selected shifts. The average SEs were similar in both stress groups (HJS 89%, range 82–94% vs. LJS 89% range 84–95%). SE varied very little in connection with different work shifts, being highest after night shifts (HJS 88%, range 81–94% vs. LJS 90%, range 79–96%).

Average sleep latencies were similar during the field measurements (HJS 0:06h, LJS 0:05h,  $p<0.47$ ) and in connection with different work shifts and days off ( $p$ -values  $>0.13$ ).

Table 9. Sleep length and efficiency by actigraphy in connection with different work shifts.

	Sleep length (h)				Reduced sleep efficiency ( $\leq 85\%$ )			
	High Job Strain		Low Job Strain		High Job Strain		Low Job Strain	
	Mean	(Min-max)	Mean	(Min-max)	P-value <sup>1</sup>	%	(n)	P-value <sup>2</sup>
The 3-week period	06:46	(04:52–07:51)	06:51	(04:54–08:22)	0.76	17	(7)	0.36
Before morning shifts	05:49	(04:10–07:03)	06:05	(04:02–07:42)	0.15	21	(9)	0.03
Quick returns <sup>3</sup>	05:22	(03:19–07:31)	05:50	(03:53–08:17)	0.06	14	(5)	1.00
After evening shifts <sup>4</sup>	06:13	(03:58–08:10)	06:41	(04:34–08:48)	0.08	20	(8)	0.26
After night shifts	04:12	(02:03–06:14)	04:35	(00:13–07:40)	0.11	19	(8)	0.24
After days off	07:20	(05:28–09:30)	07:20	(05:35–09:32)	0.85	14	(6)	0.59

<sup>1</sup> Mann-Whitney U-test

<sup>2</sup> Fisher's exact test

<sup>3</sup> between evening and morning shift (n=84; HJS n=37, LJS n=47)

<sup>4</sup> includes double shifts (morning and evening shift)

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The proportion of employees with insufficient sleep was 38% ( $n=16$ ) in the HJS group and 25% ( $n=13$ ) in the LJS group, although these difference did not reach statistical significance ( $p=0.15$ ). The proportion of participants who often experienced difficulties initiating sleep when working shifts, was higher in the HJS group than in the LJS group (76 vs. 42%,  $p<0.01$ ). Within shift categories, this difference was observed in connection with evening shifts (64 vs. 30%,  $p=0.01$ ). Furthermore, the proportion of participants having difficulties re-initiating sleep after waking up during the night was larger in the HJS group than the LJS group (76 vs. 55%,  $p=0.03$ ). The occurrence of any sleep disturbance at least 2–4 times a week was somewhat higher in the HJS group (77%), than in the LJS group (59%); a difference approaching statistical significance ( $p=0.06$ ). The ESS mean scores were similar in both job strain groups (HJS 8.6 and LJS 7.6,  $p=0.20$ ) similar to proportions of participants with increased daytime sleepiness (HJS 31%,  $n=13$  and LJS 32%,  $n=17$ ,  $p<0.90$ ). However, 33% ( $n=14$ ) of participants in the HJS group produced an ESS score close to the cut-point (8–9/10), compared to 15% ( $n=8$ ) in the LJS group ( $p=0.10$ ).

Taking naps was very common among the study participants; according to the sleep diaries, 93% ( $n=88$ ) of the participants took at least one nap during the three-week period and 22% ( $n=21$ ) took naps at least twice a week. The total sleep length per 24 hours increased by only a few minutes when naps were included (HJS 06:52h vs. LJS 07:00h,  $p=0.30$ ). Shift-specific sleep lengths of main sleep periods showed no significant difference between nappers and non-nappers; nappers slept on average 5 minutes longer before a morning shifts and 15 minutes longer after a night shifts.

Napping before the first night shift was common, and the proportion of nappers was higher in the LJS than in the HJS group (72 vs. 45%;  $p<0.01$ ). The average nap duration before a night shift was shorter in the HJS group than in the LJS group (35 vs. 62min,  $p=0.01$ ). The frequencies or durations of naps showed no other statistical differences between the stress groups (Table 10). Less than one third (29%,  $n=18$ ) of those who worked at least two consecutive night shifts took naps between the night shifts. Taking naps during the night shift was unusual, as only 4% slept on duty at least once.

Table 10. The proportions of nappers and average durations of naps.

	Napping frequency				Nap duration (min)							
	High		Low		High		Low					
	Job Strain		Job Strain		Job Strain		Job Strain					
	%	(n)	%	(n)	P-value <sup>1</sup>	Mean	SD	Mean	SD	DF	T-value	P-value
Nappers <sup>2</sup>	91	(38)	94	(50)	0.70	37	(42)	45	(31)	93	-1.12	0.26 <sup>3</sup>
After morning shift	67	(28)	59	(31)	0.52	18	(31)	17	(24)	93	0.24	0.81 <sup>3</sup>
Before 1 <sup>st</sup> night shift	45	(19)	72	(38)	<0.01	35	(59)	62	(68)	-	-	0.01 <sup>4</sup>
On a day off	67	(28)	64	(34)	0.80	21	(29)	29	(35)	93	-1.05	0.30 <sup>3</sup>

<sup>1</sup> Pearson  $\chi^2$

<sup>2</sup> at least once during 3-week measurement

<sup>3</sup> independent samples T-test

<sup>4</sup> Mann-Whitney U-test

### 8.3.2 Sleepiness and alertness

There was a higher number of morning shifts with ratings of severe sleepiness ( $KSS \geq 7$ ) at the beginning or the end of the shift in the HJS group than in the LJS group (1.7 vs. 0.8,  $p=0.01$ ,  $p$  adjusted  $<0.01$ ) and a larger proportion of severe sleepiness ratings in connection with quick returns (Table 11). In general, the KSS ratings were lowest at the beginning of evening shifts (HJS 3.5 vs. LJS 3.3,  $p=0.38$ ) and highest at the end of night shifts (HJS 6.6 vs. LJS 6.8,  $p=0.54$ ), with no differences between the two groups.

**Table 11. Shift-specific proportions of participants with severe sleepiness ( $KSS \geq 7$ ) at least once.**

	High Job Strain		Low Job Strain		P-value <sup>1</sup>	$\chi^2$ value	P-value <sup>2</sup>
	%	(n)	%	(n)			
All shifts	80	(31)	86	(42)	0.44	0.60	0.30
Morning shifts	51	(20)	50	(25)	0.90	0.01	0.41
Evening shifts	28	(11)	33	(16)	0.60	0.28	0.43
Night shifts	69	(27)	76	(37)	0.51	0.43	0.37
Quick returns <sup>3</sup>	26	(10)	8	(4)	0.04	4.96	0.03

<sup>1</sup> Pearson  $\chi^2$

<sup>2</sup> logistic regression analysis, education as a covariate

<sup>3</sup> between evening and morning shift ( $n=84$ ; HJS  $n=37$ , LJS  $n=47$ )

The mean PVT reaction times (RT) were similar in both job strain groups. The mean RT's at different measurement points were mostly slight  $<300$ ms ( $p$ -values  $>0.29$  for job strain group difference), but during the night shift the mean RT was  $>300$ ms in the HJS group ( $p=0.14$ ) (Figure 11). Napping before or during the night shift before the PVT test had no effect on the results.

The proportion of participants with at least one PVT lapse during a night shift was higher in the HJS group than in the LJS group (40 vs. 26%,  $p=0.02$ , adjusted with education). There were no other statistically significant differences in the occurrence of lapses in PVT tests



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on workdays. However, the day off test showed a higher proportion of participants with at least one lapse in the HJS group (39 vs. 20%,  $p=0.03$ ) (Figure 11), but the difference was not statistically significant with education as a covariate.

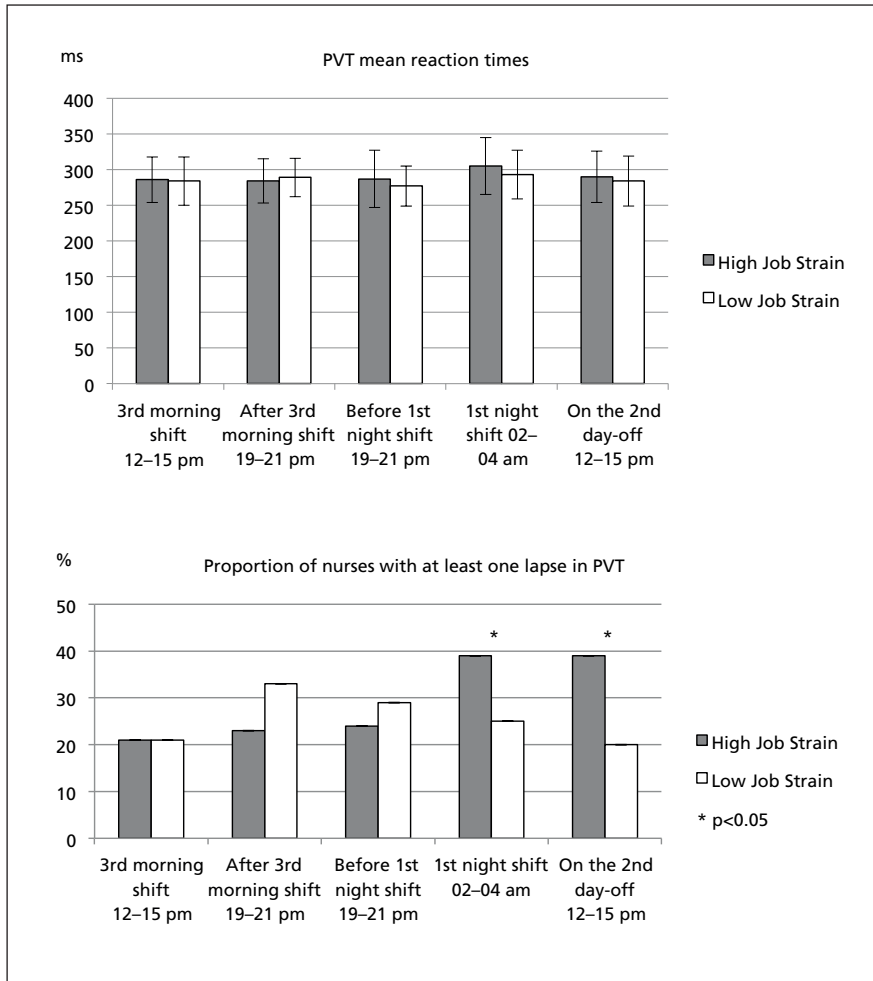


Figure 11. PVT mean reaction times with standard deviations and proportions participants with at least one PVT lapse in pre-selected shifts.

## **8.4 Perceived workload and recovery from previous work shift**

In general, the perceived mental workload was at least “somewhat too high” for one third of the HJS group, and the physical workload was at least “somewhat too high” for one quarter of them. Both of these proportions were higher than in the LJS group ( $p < 0.01$ ;  $p = 0.04$  respectively). Within shift types, the HJS group more often reported high mental workload in the morning and night shifts but not in the evening shifts. Physical workload was perceived as being too high more often in the HJS group in the morning shifts and with education as a covariate also in the night shifts (Table 12).

Average ratings of recovery from the previous shift were poorer in the HJS group in connection with all work shifts and morning shifts (Table 12). The majority (60%,  $n = 53$ ) of all participants experienced poor or non-existent recovery during the daytime sleep following a night shift. The recovery ratings also showed a larger proportion of good (complete or nearly complete) recovery in the LJS group than HJS group from all work shifts (49 vs. 19%,  $p < 0.01$ ) and evening shifts (43 vs. 31%,  $p = 0.04$ ). Poor recovery from the previous work shift was more common in the HJS group than the LJS group in connection with evening shifts (38 vs. 15%,  $p < 0.02$ ). However, there were no significant work stress group differences in connection with morning or night shifts or quick returns ( $p > 0.23$ ).

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**Table 12. Shift-specific proportions of participants with high perceived physical and mental workload, severe sleepiness and average subjective recovery from a previous work shift.**

	High Job Strain		Low Job Strain		P-value <sup>1</sup>	χ <sup>2</sup> value	P-value <sup>2</sup>	
	%	(n)	%	(n)				
High <sup>3</sup> mental workload								
All shifts	33	(14)	9	(5)	<0.01	9.44	<0.01	
Morning shifts	33	(14)	17	(9)	0.02	7.43	0.04	
Evening shifts	21	(9)	12	(6)	0.30	4.79	0.29	
Night shifts	47	(18)	22	(11)	<0.05	7.88	0.02	
Quick returns <sup>4</sup>	31	(11)	20	(9)	0.50	2.35	0.35	
High <sup>3</sup> physical workload								
All shifts	24	(10)	6	(3)	0.04	6.57	<0.01	
Morning shifts	31	(13)	6	(3)	<0.01	11.85	<0.01	
Evening shifts	17	(7)	10	(5)	0.11	7.47	0.09	
Night shifts	40	(15)	18	(9)	0.09	8.04	<0.01	
Quick returns <sup>4</sup>	25	(9)	17	(8)	0.55	3.02	0.26	
	Mean	(SD)	Mean	(SD)	P-value <sup>6</sup>	Df	T-value	P-value <sup>2</sup>
Subjective recovery <sup>7</sup>								
All shifts	2.9	(0.7)	2.5	(0.7)	0.01	93	2.56	<0.01
Morning shifts	2.6	(0.7)	2.2	(0.8)	0.02	93	2.47	<0.01
Evening shifts	2.9	(1.1)	2.5	(0.9)	0.07	93	1.86	0.05
Night shifts	3.6	(1.1)	3.5	(1.0)	0.94	87	0.08	0.26
Quick returns <sup>3</sup>	4.0	(2.2)	3.4	(2.3)	0.25	92	1.15	0.16

<sup>1</sup> Pearson Chi-Square

<sup>2</sup> logistic regression analysis, education as a covariate

<sup>3</sup> mental and physical workload scale from much too low to much too high

<sup>4</sup> morning shift(s) after an evening shift(s)

<sup>5</sup> Karolinska Sleepiness Scale  $\geq 7$

<sup>6</sup> independent samples T-test

<sup>7</sup> recovery scale from 1=complete to 5=not at all

During the recovery-controlled shifts, the HJS group more often perceived their mental workload to be too high compared to the LJS group during the first night shift (56 vs. 24%,  $p<0.01$ ). There was, however, no difference between the groups in subjective recovery ( $p=0.25$ ). There were no job strain group differences in mental or physical workload or recovery during the third consecutive morning shift ( $p>0.20$ ).

### **8.5 Heart rate variability**

#### **8.5.1 HRV parameters during 30 minutes before sleep**

The studied HRV parameters, the mean heart rate (HR), the high and low frequency power (HF and LF, consequently), the high-to-low frequency ratio (LF/HF ratio) and the RMSSD (root mean square of the differences between successive inter beat intervals) showed no statistically significant job strain group differences (Figure 12). In a similar manner, in both job strain groups, mean HR was highest and HF power lowest before going to sleep after a night shift (Table 13).

Table 13. Results of HRV parameters during 30 minutes before sleep.

		Low Job Strain			High Job Strain			P -value <sup>1</sup>	Adjusted P <sup>2</sup>
		Mean	SD	95% CI	Mean	SD	95% CI		
Heart Rate (beats per minute)	Morning shift	75.33	(7.43)	73.15–77.44	72.45	(9.78)	69.31–75.55	0.17	0.82
	Night shift	80.93	(13.03)	77.02–85.15	79.17	(9.66)	76.06–82.31	0.17	0.82
	Day-off	76.89	(11.63)	73.56–80.63	73.06	(11.31)	69.69–77.44	0.18	0.82
High Frequency power log (ms <sup>2</sup> )	Morning shift	5.84	(0.76)	5.61–6.06	5.71	(1.29)	5.25–6.08	0.81	1.00
	Night shift	5.38	(1.52)	4.98–5.96	5.46	(0.82)	5.21–5.74	0.86	1.00
	Day-off	5.78	(1.39)	5.39–6.24	5.74	(1.15)	5.34–6.11	0.80	1.00
Low Frequency power log (ms <sup>2</sup> )	Morning shift	6.79	(0.74)	6.54–6.98	6.61	(0.90)	6.26–6.85	0.38	0.94
	Night shift	6.52	(0.95)	6.24–6.84	6.63	(0.69)	6.39–6.84	0.77	1.00
	Day-off	6.74	(0.99)	6.45–7.04	6.62	(0.92)	6.27–6.91	0.75	1.00
LF/HF ratio	Morning shift	3.35	(1.77)	2.89–3.91	3.65	(2.35)	2.99–4.52	0.68	1.00
	Night shift	4.56	(2.97)	3.64–5.51	4.18	(2.12)	3.57–4.90	0.26	0.86
	Day-off	3.71	(2.45)	3.02–4.53	3.35	(2.09)	2.78–4.20	0.81	1.00
RMSSD <sup>3</sup> (ms)	Morning shift	31.75	(11.04)	28.72–35.12	33.62	(19.82)	27.48–40.58	0.87	1.00
	Night shift	32.74	(28.33)	25.73–45.52	27.46	(13.78)	23.75–32.74	0.51	0.98
	Day-off	36.56	(26.21)	29.92–46.51	33.40	(18.02)	28.22–40.70	0.82	1.00

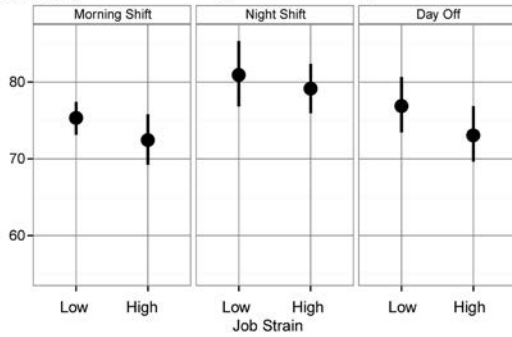
<sup>1</sup> Wilcoxon rank sum test

<sup>2</sup> minP adjustment method

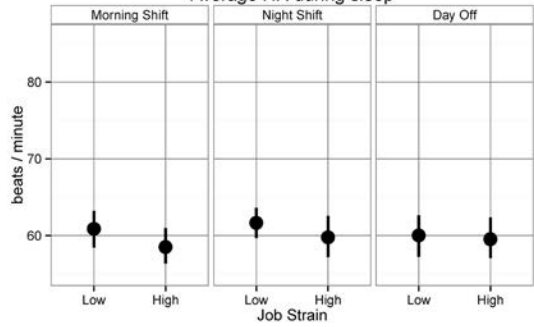
<sup>3</sup> the square root of the squared mean of the differences between successive IBIs

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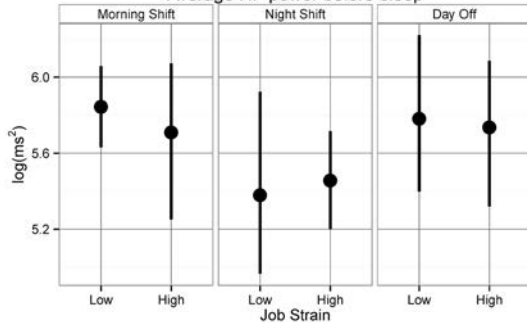
beats / minute      Average HR before sleep



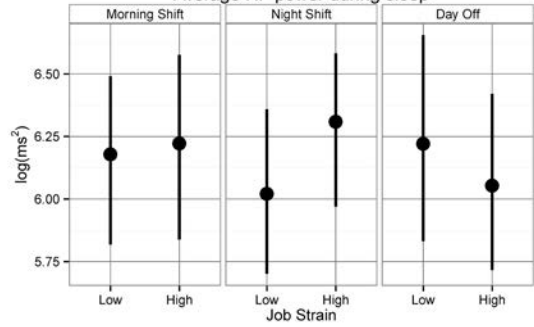
Average HR during sleep



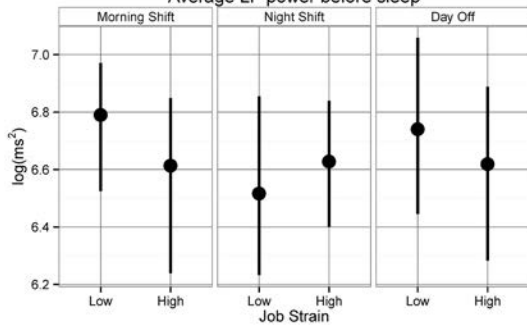
Average HF power before sleep



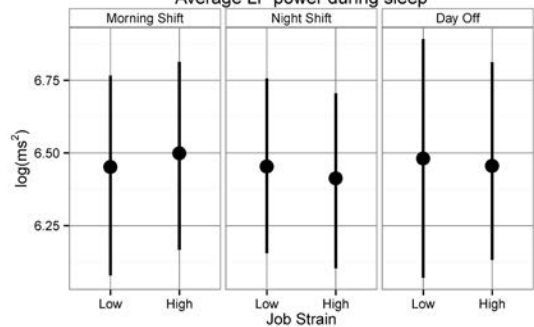
Average HF power during sleep



Average LF power before sleep



Average LF power during sleep



## 8 RESULTS

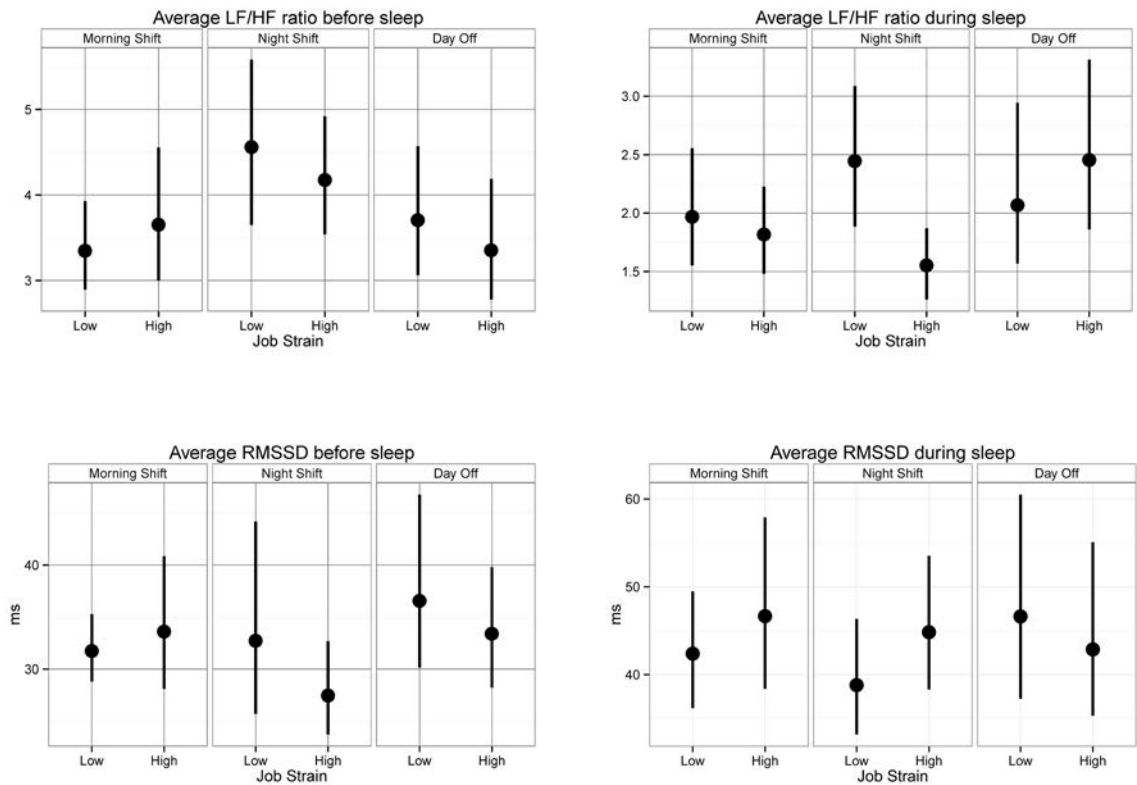


Figure 12. Average heart rates (HR), high and low frequency (HF, LF), LF/HF ratio, and RMSSDs for the high and low job strain groups before sleep and during sleep. Vertical lines represent 95% bootstrap confidence intervals for the mean.

### **8.5.2 HRV parameters during 30 minutes of lowest heart rate**

During the 30-minute period of lowest heart rate, the studied HRV parameters (mean HR, HF power, LF power, LF/HF ratio and RMSSD) differed between day off and the two work shifts in other parameters (p-values <0.01, data not shown) except for the LF/HF-ratio (p-values 0.06–0.09). There were no statistically significant job strain group differences during the sleep. (Table 14.)



Table 14. Results of HRV parameters during the 30-minute period of lowest HR during sleep.

		Low Job Strain			High Job Strain			P-value <sup>1</sup>	Adjusted P <sup>2</sup>
		Mean	SD	95% CI	Mean	SD	95% CI		
Heart Rate (beats per minute)	Morning shift	60.88	(7.36)	58.36–63.29	58.52	(6.77)	56.44–60.81	0.11	0.59
	Night shift	61.67	(6.31)	59.48–63.62	59.79	(7.90)	57.12–62.39	0.15	0.69
	Day-off	60.02	(7.81)	57.32–62.49	59.54	(7.69)	57.31–62.40	0.22	0.79
High Frequency power log (ms <sup>2</sup> )	Morning shift	6.18	(1.04)	5.83–6.50	6.22	(1.13)	5.83–6.59	0.59	0.98
	Night shift	6.02	(1.01)	5.71–6.34	6.31	(0.90)	5.99–6.59	0.62	0.98
	Day-off	6.22	(1.26)	5.84–6.67	6.05	(1.04)	5.71–6.40	0.35	0.91
Low Frequency power log (ms <sup>2</sup> )	Morning shift	6.45	(1.31)	6.09–6.76	6.50	(0.99)	6.18–6.82	0.53	0.98
	Night shift	6.45	(0.91)	6.16–6.76	6.41	(0.86)	6.13–6.71	0.57	0.98
	Day-off	6.48	(1.22)	6.08–6.88	6.46	(0.99)	6.14–6.80	0.33	0.90
LF/HF ratio	Morning shift	1.97	(1.53)	1.54–2.55	1.82	(1.14)	1.49–2.23	0.66	0.98
	Night shift	2.45	(1.87)	1.91–3.14	1.55	(0.91)	1.27–1.87	0.08	0.51
	Day-off	2.07	(1.92)	1.57–2.88	2.46	(2.09)	1.88–3.28	0.79	0.98
RMSSD <sup>3</sup> (ms)	Morning shift	42.40	(20.39)	36.24–49.56	46.67	(29.39)	38.54–58.57	0.70	0.98
	Night shift	38.82	(19.82)	32.91–46.47	44.85	(22.00)	38.57–53.20	0.69	0.98
	Day-off	46.64	(33.41)	37.24–60.42	42.89	(28.05)	35.15–55.00	0.48	0.98

<sup>1</sup> Wilcoxon rank sum test  
<sup>2</sup> minP adjustment method  
<sup>3</sup> the square root of the squared mean of the differences between successive IBIs

### **8.5.3 Differences in HRV parameters before sleep and during sleep**

When calculating the differences in HRV parameters during the 30 minutes before sleep and during the 30-minute period of lowest HR during sleep, the mean HR decreased more in the HJS group compared to the LJS group ( $p < 0.05$ ). However, in multiple adjusted analyses, the difference was not statistically significant. The RMSSD was lower in the HJS group during daytime sleep after a night shift than in the LJS group ( $p < 0.02$ ), but, similarly, the adjusted analysis eliminated this difference. There were no statistically significant job strain group differences in the other HRV parameters. (Table 15.)

Table 15. Differences in HRV parameters during 30 minutes before sleep and during the 30-minute period of lowest HR during sleep.

		Low Job Strain			High Job Strain				
		Mean	SD	95% CI	Mean	SD	95% CI	P-value <sup>1</sup>	Adjusted p <sup>2</sup>
Heart Rate (beats per minute)	Morning shift	13.30	(7.78)	10.90–15.91	11.82	(7.60)	9.15–14.19	0.26	0.90
	Night shift	20.25	(12.29)	16.79–24.80	19.02	(11.93)	14.81–22.88	0.52	0.99
	Day-off	14.45	(8.55)	12.12–17.88	11.18	(7.84)	8.73–14.00	0.05	0.40
High Frequency power log (ms <sup>2</sup> )	Morning shift	-0.42	(1.09)	-0.74–0.03	-0.35	(0.82)	-0.65–0.10	1.00	1.00
	Night shift	-0.78	(1.27)	-1.19–0.34	-0.85	(0.95)	-1.15–0.53	0.35	0.95
	Day-off	-0.47	(1.04)	-0.81–0.13	-0.36	(1.02)	-0.69–0.11	0.71	0.99
Low Frequency power log (ms <sup>2</sup> )	Morning shift	0.20	(1.13)	-0.20–0.54	0.21	(1.01)	0.11–0.54	0.51	0.99
	Night shift	0.08	(1.21)	-0.31–0.48	0.19	(1.01)	-0.15–0.53	0.70	0.99
	Day-off	0.17	(1.05)	-0.18–0.51	0.14	(1.19)	-0.24–0.52	0.42	0.97
LF/HF ratio	Morning shift	1.31	(2.11)	0.66–2.09	1.25	(1.67)	0.73–1.84	0.51	0.99
	Night shift	2.32	(2.75)	1.42–3.26	2.39	(2.05)	1.70–3.07	0.57	0.99
	Day-off	1.46	(2.61)	0.69–2.47	0.81	(2.50)	0.07–1.75	0.13	0.69
RMSSD <sup>3</sup> (ms)	Morning shift	-11.95	(17.50)	-18.48–7.06	-11.06	(22.42)	-19.86–4.66	0.84	0.97
	Night shift	-9.85	(22.51)	-17.05–2.42	-19.14	(20.64)	-27.13–13.31	0.04	0.32
	Day-off	-11.01	(22.92)	-18.41–4.01	-9.99	(22.46)	-18.42–3.39	0.59	0.99

<sup>1</sup> Wilcoxon rank sum test

<sup>2</sup> minP adjustment method

<sup>3</sup> the square root of the squared mean of the differences between successive IBIs

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### 8.5.4 HR profiles during first 4 hours of sleep

HR profiles during the first 4 hours of sleep were similar in both job strain groups after morning and night shifts and day off (Figure 13).

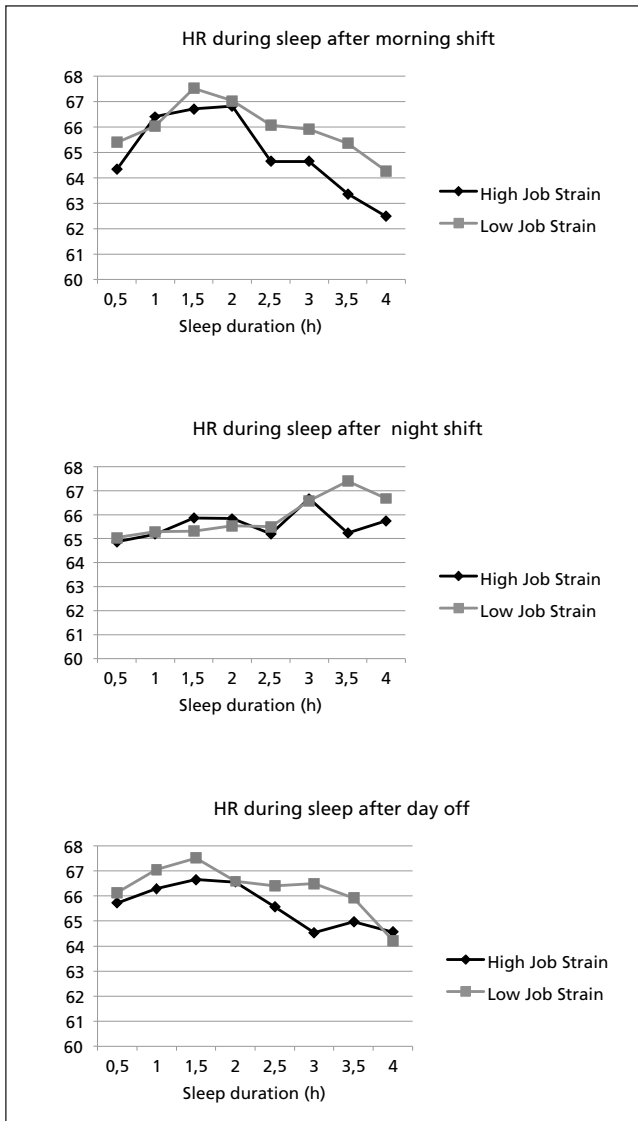


Figure 13. Heart rate profiles during first 4 hours of sleep.

### **8.6 Stress biomarkers**

Three participants were excluded from the analysis of the cortisol results due to 1) asthma medication including cortisone with long-term effect, 2) medication for a rheumatic disease, and 3) inexplicably high cortisol values. One participant was excluded from the analysis of the sAA results due to medication for a rheumatic disease.

#### **8.6.1 Acute stress reactivity**

There was no job strain group difference in the salivary cortisol or AA levels in the baseline sample (Table 16). The TSST caused, on average, a 2.27-fold increase in the salivary cortisol concentration in the HJS group and a 1.48-fold increase in the LJS group. The TSST1–3 stress biomarker levels showed no statistically significant job strain group differences (Table 16).

Table 16. Salivary cortisol and alpha-amylase levels in laboratory study with Trier Social Stress Test (TSST).

	Low Job Strain			High Job Strain		
	n	Mean	(Min-max)	n	Mean	(Min-max)
Cortisol (nmol/l)						
Baseline <sup>4</sup>	47	10.85	(4.25–38.70)	41	9.75	(4.00–46.16)
TSST1 <sup>5</sup>	50	10.20	(1.90–30.61)	42	9.64	(4.18–49.29)
TSST2 <sup>6</sup>	50	13.49	(4.08–35.40)	40	13.34	(5.33–38.27)
TSST3 <sup>7</sup>	50	15.27	(5.50–51.05)	41	15.58	(5.43–39.68)
Alpha-amylase (U/ml)						
Baseline <sup>4</sup>	48	108.19	(9.18–384.66)	41	142.90	(4.92–436.24)
TSST1 <sup>5</sup>	52	119.71	(7.54–396.90)	41	137.41	(6.89–349.98)
TSST2 <sup>6</sup>	51	163.11	(9.84–344.73)	41	179.19	(7.19–471.66)
TSST3 <sup>7</sup>	52	145.04	(6.56–678.96)	41	149.00	(9.84–398.34)
					P-value <sup>1</sup>	P-value <sup>2</sup>
						P-value <sup>3</sup>

<sup>1</sup> ANOVA for log transformed distribution  
<sup>2</sup> education as a covariate  
<sup>3</sup> physical activity as a covariate  
<sup>4</sup> after arriving to the laboratory  
<sup>5</sup> at the beginning of the TSST  
<sup>6</sup> at the end of the TSST  
<sup>7</sup> 15 minutes after completing the TSST

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The profiles of salivary cortisol and AA did not show job strain group differences during or after the TSST (Figure 14). There was a sharp rise in the cortisol concentration in the HJS group, but the difference remained below statistical significance ( $p < 0.09$ ) compared to the LJS group, also with education as a covariate. The total secretion of salivary cortisol or AA calculated as area under the curve ( $AUC_g$ ) was similar in the TSST and in the laboratory measurement day (baseline + TSST) in both job strain groups ( $p > 0.22$ , data not shown). Salivary AA over cortisol ratios also demonstrated a similarity between the two job strain groups ( $p > 0.33$ , data not shown).

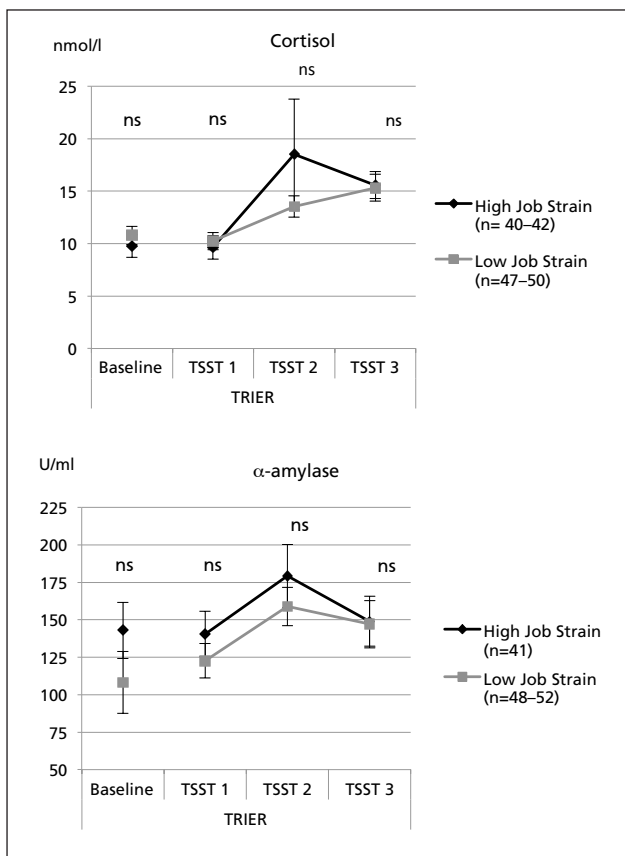


Figure 14. Salivary cortisol and alpha-amylase profiles in Trier Social Stress Test. Vertical lines represent SEM (standard error of mean). Ns = non-significant statistical difference between the job strain groups.

### **8.6.2 Salivary cortisol in field measurements**

There were no stress group differences in salivary cortisol levels on awakening (AW), at 30 minutes after awakening (AW30) or before going to sleep after a morning shift, night shift and day off day (Table 17). The magnitude of salivary cortisol awakening response (CAR) was on average 51% in the HJS group and 50% in the LJS group on the morning shift, 31% and 30% on the night shift (p-values >0.76), but 32% and 40% on the day off (p-value =0.17 for group difference, <0.05 with education as a covariate).



Table 17. Salivary cortisol levels (nmol/l) during field measurements.

	Low Job Strain			High Job Strain		
	n	Mean	(Min-max)	n	Mean	(Min-max)
Morning shift						
Awakening	49	10.41	(2.57–33.66)	41	11.14	(5.45–20.10)
30min after awakening	49	22.86	(6.67–48.48)	42	24.98	(6.17–58.48)
In the evening (22 pm)	47	2.93	(0.57–11.72)	39	2.90	(0.42–18.05)
Night shift						
Awakening	49	12.81	(1.20–26.25)	41	12.83	(5.24–27.57)
30min after awakening	50	21.22	(1.04–53.79)	41	20.31	(6.56–42.74)
In the morning (08 am)	49	11.84	(0.73–31.75)	42	11.57	(4.64–18.44)
Day off						
Awakening	50	14.33	(3.54–33.15)	42	13.66	(6.46–29.04)
30min after awakening	49	24.24	(8.58–53.95)	42	21.82	(10.84–40.56)
In the evening (22 pm)	48	3.94	(0.50–48.74)	41	2.24	(0.50–9.87)

<sup>1</sup> ANOVA for log transformed distribution

<sup>2</sup> education as a covariate

<sup>3</sup> physical activity as a covariate

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The evening declines were similar in both stress groups (Figure 15). In connection with morning shifts, the evening values of salivary cortisol were elevated in 23% (n=9) of the participants in the HJS group and 29% (n=14,  $p=0.63$ ) in the LJS group. After a day off, the proportions of elevated cortisol levels were 27% (n=11) in the HJS group and 32% (n=16,  $p=0.65$ ) in the LJS group.

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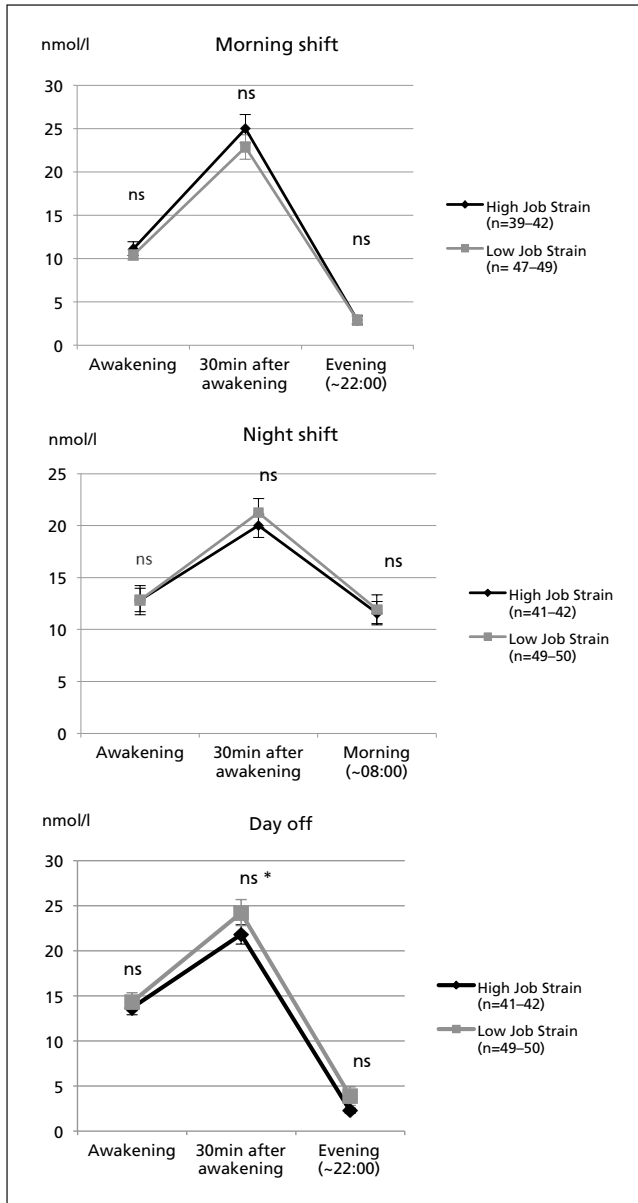


Figure 15. Salivary cortisol profiles on measurement days. Vertical lines represent SEM (standard error of mean). Ns = non-significant statistical difference between job strain groups. \* = significant with education as a covariate.

### **8.6.3 Salivary alpha-amylase in field measurements**

In the morning shift, 30 minutes after awakening (AW30), salivary AA levels were higher in the HJS group than in the LJS group. There were no other significant differences in average sAA levels during the morning shift, night shift or day off -measurements (Table 18).

After waking up, there was a similar dip in sAA levels in both job strain groups ( $p$ -values  $\geq 0.14$ ) (Figure 16). A similar elevation in the evening levels was also detected in both groups.

Table 18. Salivary alpha-amylase levels (U/ml) during field measurements.

	Low Job Strain			High Job Strain		
	n	Mean	(Min-max)	n	Mean	(Min-max)
Morning shift						
Awakening	50	90.71	(5.58–395.57)	41	114.90	(2.95–393.27)
30min after awakening	48	31.02	(6.23–119.06)	39	49.83	(3.61–269.62)
In the evening (22 pm)	51	81.97	(2.30–266.66)	42	93.16	(2.95–272.57)
Night shift						
Awakening	52	79.77	(2.95–357.52)	39	92.88	(3.61–386.06)
30min after awakening	50	43.08	(5.58–161.70)	40	52.60	(6.89–168.59)
In the morning (08 am)	51	88.63	(2.95–596.96)	42	80.98	(3.61–366.05)
Day off						
Awakening	51	78.20	(4.43–248.05)	41	112.46	(3.94–487.41)
30min after awakening	49	38.51	(2.62–105.62)	41	46.34	(2.95–193.85)
In the evening (22 pm)	52	117.28	(3.61–347.68)	42	110.42	(5.90–457.88)

<sup>1</sup> ANOVA for log transformed distribution

<sup>2</sup> education as a covariate

<sup>3</sup> physical activity as a covariate

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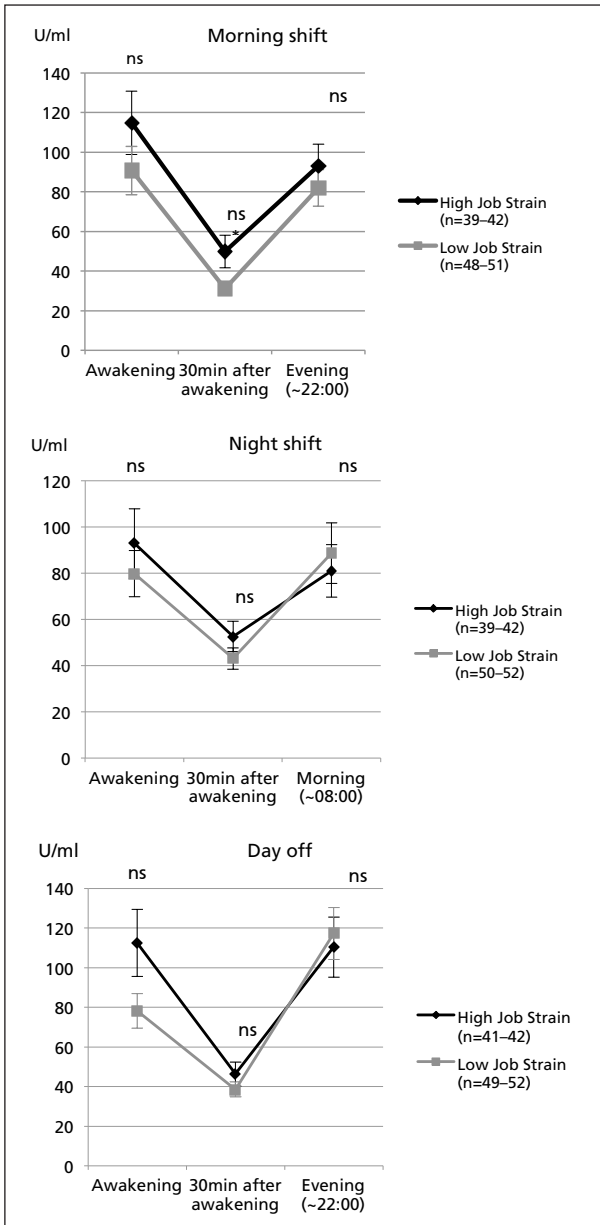


Figure 16. Salivary alpha-amylase profiles in measurement days. Vertical lines represent SEM (standard error of mean). Ns = non-significant statistical difference between job strain groups. \* = significant with education as a covariate.

## **9 DISCUSSION**

This study examined the association of job strain with sleep and psychophysiological functioning and recovery in shift working health care professionals. The sample group of female nurses and nursing assistants was recruited from an on-going epidemiological study. The threshold for exposure to a stressful work environment was defined as having worked at least three years on the same ward. To increase contrast between the job strain groups, only the top and bottom quartiles of job strain were included in the study. Studies I–III which measured sleep, working times and heart rate variability were field studies. Study IV, including stress biomarkers, was conducted in both the field and the laboratory.

### **9.1 Results in relation to job strain**

#### **9.1.1 Working times and workload**

The actual total working hours was close to the collective agreement of the Finnish public sector employees of 114:45h in 3 weeks (The Trade Union for the Public and Welfare Sectors JHL, 2014) and was similar in both job strain groups. This was contrary to the study (Study II) hypotheses of an association of job strain with extended working hours. Earlier international results (de Castro et al., 2012; Geiger-Brown et al., 2012; Rogers et al., 2004; Scott et al., 2006; Wu et al., 2013) have shown that overtime work and extended shifts are common in the health care sector. In this data 8% of the work shifts exceeded 12 hours, compared to, for example, 67% of the shifts in Scott et al. (2006). However, shift schedules in this study differed between the job strain groups in some characteristics. The HJS group had more single days off and quick returns

to work than the LJS group, which, in turn, had somewhat longer night shifts and more frequent extended shifts. Also consecutive extended shifts were more common in the LJS group, but this result was due to the small group size of this subgroup ( $p=0.06$ ,  $n=37$ ).

The majority (59%) of the evening shifts were followed by a quick return to a morning shift. Moreover, the shift interval in quick returns was, on average, less than ten hours. Shift intervals with less than 11 hours are related to increased sleep and sleepiness problems (Åkerstedt, 2003). The increased sleepiness reported with quick returns, points to an obvious need for longer recovery periods between shifts. The minimum shift interval determined by the Finnish Occupational Safety Act is 9 hours. In addition, the new act ("laki työturvallisuuden muuttamisesta 329/2013 [Law concerning the change of Occupational Safety Act 329/2013]," 2013) also requires a risk assessment of the working time arrangement. To decrease work stress and consequently, poor recovery, it would be important to reduce quick returns by improving shift schedules. In an intervention study, reducing quick returns, improved the sleep, alertness and well-being of health care workers' (Hakola et al., 2010). At the very least, the inter-shift recovery time should be extended to a minimum of 11 hours as FIOH recommends (Finnish Institute of Occupational Health, 2014). Although more prevalent in the LJS group, extended shifts and consecutive extended shifts also cause insufficient sleep (Kecklund et al., 2001), and they should therefore be avoided. Compared to international studies (Borges & Fischer, 2003, Scott et al., 2006) the proportion of extended shifts was very small in this data.

Another unfavourable work shift pattern in the HJS group was a higher number of single days off compared to the LJS group. Single days off can be non-restorative, but studies on this issue are rare. Garde et al. (2012) reported that self-rostering among care-givers resulted in a decreased number of single days off. On the other hand, being able to have more influence on one's work schedule can also increase fatigue due to a preference for continuous free time by increasing, for example, quick returns (Kandolin & Huida, 1996).

The HJS group was not able to influence their working hours as much as the LJS group. It appears that control over working times may alleviate various work demands during working hours and subsequently facilitate recovery. Workers with good work time control have lower levels



of symptoms of insomnia, fatigue and depression than workers with poor control over their working times. (Takahashi et al., 2012.) Moreover, poor working time control increases the risk of more absences due to sickness (Ala-Mursula et al., 2002) and disability pensioning (Vahtera et al., 2010). However, comparing nurses' reported work time control in other countries indicates that even in the HJS group the opportunities to influence working hours were relatively high (Aiken et al., 2001; Nabe-Nielsen et al., 2010).

In line with Karasek's work-stress model (Karasek et al., 1998), the HJS group perceived a higher mental and physical workload than the participants in the LJS group. The association of work stress with workload was strongest during the morning and night shifts, as well as during pre-selected similar shift arrangements. The results suggest that the high job demand component of the work-stress model is closely interconnected with a high perceived workload. During the naturally occurring shift arrangements, HJS was associated with poorer recovery from all work shifts. However, during the pre-selected, similar shift arrangements, work stress was not associated with subjective recovery, suggesting that the differences in recovery were at least partly related to differences in shift characteristics. In this study, subjective recovery was lowest in shift combinations that included short periods of time-off before the shifts. This was in accordance with Axelsson et al. (2004).

### **9.1.2 Sleep quality, sleepiness and alertness**

In concordance with the study hypothesis (Study I) and earlier research (Groeger et al., 2004), shortened sleep and sleep disturbances were highly prevalent among shift workers. The participants in both job strain groups slept, on average, almost an hour (0:49) less than Finnish women on average (7.62 h) (Kronholm et al., 2006). Other studies have also reported similar average sleep durations: over 7 hours for females by both survey- and EEG-based measurements (Groeger et al., 2004; Hume, Van, & Watson, 1998). The total amount of sleep increased by only a few minutes with self-reported naps added to the average sleep length: likewise in Ruggiero and Redeker (2014). There appeared to be continuous sleep deprivation in the nursing staff studied, as the questionnaire-based proportion of sleep deprived personnel was around one third of the participants.

Sleep efficiencies (SE) were mostly high and sleep latencies short in both job strain groups. This corresponds with earlier findings that shift workers tend to have a good sleep propensity and consolidation (Åkerstedt & Wright, 2009). However, the HJS group, more often than the LJS group, showed reduced sleep efficiency before morning shifts. This is in line with earlier results that anticipation of or preoccupation with high work demands the next day, impair sleep quality (Kecklund & Åkerstedt, 2004; Åkerstedt, 2006).

Sleep difficulties were very common in this sample of shift workers: approximately twice as common compared to the Finnish general population (Kronholm et al., 2008) or almost three times as common compared to Finnish female municipal employees (Lallukka et al., 2010). Job strain related sleep difficulties were attributable to stressful situations, especially difficulties initiating sleep after an evening shift. Sleep difficulties after an evening shift are probably due to work rumination (Kompier et al., 2012) and inability to relax after a stressful shift that ends too close to sleep (Hall et al., 2007).

Importantly, the HJS group was associated with fewer and shorter naps before the first night shift and more PVT lapses during the first night shift. The proportion of employees that took a nap before the first night shift was high in this study (Study I), compared to a study among midwives, where 40% of the night shifts were preceded by naps (Tremaine et al., 2013). Likewise, in Härmä et al. (1989), 56% of nurses and nursing assistants took a nap in a similar shift system. The proportion of nappers between two consecutive night shifts was lower (29%), but similar to an estimation that approximately one third of shift workers nap between consecutive night shifts in the evening before the shift (Åkerstedt, 2003; Åkerstedt et al., 2008).

Sleepiness at work was highest in connection with morning and night shifts, corresponding to a review of earlier research (Sallinen & Kecklund, 2010). This data showed that two thirds of the participants reported severe sleepiness during the first night shift, as found in another study of three-shift nurses (Flo et al., 2013). In this study (Study II), over 80% of the participants experienced severe sleepiness at work at least once during the field measurements, and 14% of all KSS ratings exceeded the threshold of severe sleepiness. In a study of hospital nurses by Geiger-Brown et al. (2012), KSS was measured at two-hour intervals

during a shift. The occurrence of high level sleepiness was found to be 45% in the three shifts. It was also found that the average KSS scores were systematically lower than those in the current study, emphasizing the high level of sleepiness among the nurses and nursing assistants. It is also important to note that light exposure during night shifts and possibly also social interactions may have an influence on the KSS ratings, reducing them by 1–2 units (Åkerstedt et al., 2014). However, there is a clear circadian phase effect on sleepiness, in which the risk for sleepiness is 6–14 times higher during night shifts compared to other shifts (Härmä et al., 2002).

Research on the associations between work stress and alertness is scarce. Ruggiero et al. (2012) found no differences between nurses working a night shift or a day shift in a standard 10-minute PVT. In the current study (Study I), the occurrence of at least one lapse in PVT during a night shift was higher in the HJS group, even though a shortened 5-minute version of the test was used. Sleepiness was pronounced only in the HJS group, although the PVT's were conducted according to the circadian rhythm and recovery controlled conditions. During the three week period, only (4%) of the study subjects reported (in their sleep diaries) napping during a night shift. It appears there are no published studies about on-duty napping in Finland. In the health care sector, scheduled napping is not recommended nor prohibited during night shifts, although scheduled naps have been found to be an effective fatigue countermeasure (Davy & Gobel, 2013; Ruggiero & Redeker, 2014; Takeyama et al., 2005). Not only the HJS group with more PVT lapses, but also the LJS group with rather similar occurrence of severe sleepiness in the night shift than the HJS group, would benefit from scheduled naps.

As a whole, associations of job strain with sleep in health care staff on shifts were fewer than predicted (Studies I–II), based on earlier results (Fahlen et al., 2006; Kalimo et al., 2000; Åkerstedt, 2006). In this group of shift workers, the additional burden of job strain on sleep and alertness became evident only in specific shift combinations: before a morning shift, after an evening shift and before a night shift. It is probable that the effects of job strain on sleep may be more pronounced in day workers (Kompier et al., 2012) and workers with extended working hours (van der Hulst, 2003), rather than shift workers.

### 9.1.3 Heart rate variability during sleep

Contrary to the study hypothesis (Study III), no associations of job strain with bootstrapped HRV parameters (mean HR, HF power, LF power, LF/HF ration, RMSSD) were found before or during sleep in connection with morning shift, night shift and a day off. There are very few earlier studies associating job strain, shift work and heart rate variability (van Amelsvoort et al., 2001; Wong et al., 2012). Within these predominantly male samples, Wong et al. (2012) found a higher RMSSD as an indication of better recovery among day workers compared to rotating shift workers. Whereas, van Amelsvoort et al. (2001) found no significant differences in HRV between day and shift workers, also adjusted with job strain. There is also a shortage of studies comparing HRV among day and shift workers. In a study by Wehrens et al. (2012), day workers were found to have a higher RMSSD and LF/HF ratio, and lower HR variance than shift workers. This would indicate higher sympathetic and/or lower parasympathetic activity which thus supports the idea of an increased cardiovascular risk among shift workers. However, it remains unclear whether or not the healthy worker effect might have influenced these findings.

There are some earlier HRV studies on health care professionals, but these studies vary remarkably in data collection length and methodology. Therefore, comparison to the current study with HRV during sleep and robust statistical analysis is challenging. In a study by Lin et al. (2013) on medical interns, even extremely long working hours during a one year period did not present changes in the HRV of female physicians. In a study on shift-working nurses Chung et al. (2012), found no significant differences between regular-shift nurses and rotating-shift nurses, in terms of sleep patterns and cardiac autonomic functions during day shifts. In another study of nurses (Riese et al., 2004) HRV was not associated with work strain in a homogenous group of night shift workers. Järvelin-Pasanen et al. (2013) also found no association of nurses' perceived occupational stress with HRV either. These non-significant results are likely due to the large variation in the HRV variables, which reflect the wide individual variation in the functioning of ANS (Järvelin-Pasanen et al., 2013).

Among media workers with irregular shifts, higher heart rate variability during the first hours of sleep was associated with better subjective recovery, whilst irregular shift work doubled the risk of poor recovery (Lindholm, et al., 2012). In the current sample of shift workers, stress-related differences in physiological recovery were not found. As presented in the previous chapter (9.1.1 Working times and workload), there was a relationship between HJS and too high a perceived workload and poor inter-shift recovery. There is evidence that two consecutive days off may be sufficient for nurses to recover their sleep-related autonomic functions after a rapidly rotating clockwise three-shift schedule (Chung et al., 2012). ANS recovery from a high perceived job strain has been found to be insufficient, especially among older female employees (Ritvanen et al., 2006).

### **9.1.4 Stress biomarkers**

In the TSST, the HJS group showed a 2.27-fold increase in cortisol concentration and the LJS group a 1.48-fold increase, but the difference was not statistically significant. Similarly, the TSST results on burn out patients and healthy workers showed no group differences (De Vente et al., 2003). Since it has been repeatedly shown that TSST induces profound endocrine responses in the majority of people, and these responses are, on average, higher in males than females (Kirschbaum et al., 1993), it may be more difficult to observe group level differences in a female sample.

Contrary to the study hypotheses (Study IV), exposure to job strain was not associated with individual salivary cortisol levels or profiles in the field measurements. As stated in the previous chapter (9.1.1 Working times and workload), group differences in job strain were detected in perceived workload and inter-shift recovery. These findings did not, however, appear in the stress biomarkers. Earlier research shows that results of biomarkers and self-reports of stress may not be consistent (Fujimaru et al., 2012; Fujiwara et al., 2004). In concordance with this study (Study IV), Fujiwara et al. (2004) found that high and low job strain groups of health care providers had similar salivary cortisol concentrations during a night shift and a non-work day. In another study, high job strain among teachers was associated with significantly elevated

salivary cortisol early in the morning before a work day, compared to teachers with low job strain (Steptoe et al., 2000).

In this study (Study IV), the salivary CARs were lower in both job strain groups in the mornings before a night shift and a day off than during a morning shift. Similarly, earlier research has shown greater CARs in nurses working a morning shift than a late day shift or a night shift (Federenko et al., 2004). It is hypothesized that anticipation of the upcoming day is of major relevance for the level of the CAR (Fries et al., 2009). In nursing work, morning shifts are regarded as most hectic, and therefore both of the job strain groups could anticipate a work shift under time pressure. On the other hand, according to this data, the CARs were below the reference values in the night shift (Clow et al., 2004). According to Fries et al. (2009) this also occurred on the days off, which may be an indication of blunted CAR in both job strain groups.

In this study (Study IV) there were no job strain group related differences in total salivary cortisol or sAA secretion measured as AUC<sub>g</sub>. This is contrary to the study hypothesis and earlier results. A previous study (Sjögren, Leanderson, & Kristenson, 2006) with exactly the same field measurement time points found that a flatter diurnal cortisol rhythm was associated with high levels of psychosocial risk factors for example, cynicism and depression. In a study by Fekedulegn et al. (2012), employees predominantly on night shifts had lower saliva cortisol AUC mean values than those predominantly on afternoon or day shifts. It appears that here are no other studies using a similar study design which measures total sAA secretion among shift workers.

Contrary to the study hypothesis (Study IV) and previous studies (Rohleder & Nater, 2009; Wong et al., 2012), HJS was not associated with flatter diurnal slopes or decreased daily production of sAA. Salivary AA levels were higher in the HJS group only 30 minutes after awakening on the day of a morning shift compared to levels in the LJS group. Contrary to the hypothesis and recent results (Ali & Pruessner, 2012), the ratio of sAA to cortisol was not associated with the level of job strain. However, there were differences between these two study samples in age, gender, stress exposure, and circadian disruption.

## 9.2 Methodological aspects

Our initial aim was to recruit a sample of 150 nursing personnel from an existing larger sample of an FPS study. However, the sample size achieved was only 99. Recruiting solely by direct mail to the work places of the respondents of the FPSS 2008 survey proved to be ineffective. Extending the deadline for recruitment resulted in only a few more participants. Sample size is closely tied to statistical power, which is the ability of a study to enable detection of a statistically significant difference when there truly is one (Eng, 2003). A previous study (Wong et al. 2012) published a power analysis based on a pilot study, with the result that a sample of 250 persons would be needed to observe physiological differences between day workers and rotating shift workers. On the other hand, shift work related HRV studies reviewed by Togo & Takahashi (2009) had, on average, approximately 70 participants. Järvelin-Pasanen et al. (2013) estimated even a sample of 51 shift workers to be adequate in comparison with earlier HRV studies. Studies of cortisol awakening response and psychosocial factors were reviewed by Chida & Steptoe (2009) using an average of 91 participants.

A high participation rate is particularly important, but in this study the participation rate remained low (24%), whereas, the group of non-contact recruits was large (28%). On the other hand, those participants in the laboratory phase of the study, completed the field measurements successfully. One of the inclusion criteria was to have at least three years' work experience on the same ward, to ensure a long-term exposure to a stressful work environment. This probably reduced the number of fixed-term contract employees in the sample, as they constitute over 20% of the health care sector (Koponen, Laiho, & Tuomaala, 2012).

The statistical methods used in this study were chosen according to the study questions that aimed to explore job strain group level differences in certain variables related to sleep and recovery in shift work. The analysis of HRV parameters (Study IV) was conducted with bootstrapping to avoid random positive group differences in multiple comparisons. Bootstrapping is especially well suited to samples of limited size. Despite data of the same size or even smaller, many of the earlier studies (Chung et al., 2012; Hernandez-Gaytan et al., 2013; Järvelin-Pasanen et al., 2013; Lo et al., 2010; Ritvanen et al., 2006; Yoshizaki et al., 2013), have not



used bootstrapping in their statistical analysis. The salivary biomarkers of stress were analysed with formula area under the curve with respect to ground, instead of area under curve with respect to increase. This is due to the fact that  $AUC_g$  is more related to total hormonal output whereas,  $AUC_i$  is more related to sensitivity in changes in secretion (Pruessner et al., 2003).

The main strength of this study is its novel study design: an experimental study with both laboratory and field study of health care staff embedded in a large on-going longitudinal cohort study. This study benefitted from the measurement of exposure to a stressful job environment based on a mean score from the same ward. Assessing the psychosocial work environment in a precise and unbiased way is a major challenge in the research of psychosocial working conditions. Typically, studies on work stress have relied on subjective individual reports which may be affected by subjectivity bias, such as negative affectivity (Rugulies, 2012). This in turn, can colour one's subjective perceptions of the quality of sleep. Ward-level estimation of job strain was used to reduce the effect of subjectivity of job strain, resulting in a less biased estimate of the environmental job strain.

In most job strain studies the follow-up has been short, a year or even less, but in this study all the participants were from wards where the job strain had been measured repeatedly in 2004 and 2008. The participants' individual level of job strain was obtained from the 2008 survey. In this study of a single occupational group, high and low job strain groups did not differ as much as they do in studies on the general population or several occupational groups (Hintsanen et al., 2007; Karasek & Theorell, 1990). To reduce subjectivity bias (i.e. bias from differences in individual stress reactivity), the mean job strain score was calculated from individual responses of all respondents in the same ward.

This is apparently the first study to examine the associations of exposure to environmental job strain with salivary cortisol and AA responses among shift working nurses and nursing assistants in both laboratory and field settings. Furthermore, it is doubtful if there have been any previous studies using the TSST on health care staff. The data on working times was collected from completed rosters instead of self-report data which is commonly used (Fekedulegn et al., 2012).



The participants were all relatively healthy females working shifts, who, for example, all had similarly high levels of hurry and stressful life events. Only two of the participants scored points typical for clinical depression. The participants had, on average, shift work experience (17.7 years) similar to the Finnish health care personnel in general. During the field measurement period, the groups did not differ in the number of absences due to sickness either. It is not likely that non-measured confounding factors existed between the job strain groups.

This field data-set was of a very good quality; very few (4%) participants refused or failed to follow through with the field measurement protocol. We used both actigraphy and sleep diaries to collect the habitual sleep-length data, whereas many earlier studies have relied solely on sleep diary data (Sallinen & Kecklund, 2010). The actigraphy measurement period of three weeks was also longer in this study than in most of the other studies, where measurements have lasted mostly from 2 to 7 nights (Diez et al., 2011; Wang, Hung, & Tsai, 2011; Takahashi et al., 2014). The longer measurement period allowed conducting shift-specific analysis on the data. Actigraphy is the most appropriate non-laboratory measure of sleep (Van de Water, Holmes, & Hurley, 2011). It is known that actigraphy provides reliable results compared with polysomnography (PSG) in the evaluation of total sleep time (Delafose et al., 2000). PSG would have been an ideal method of detecting changes in sleep, as stress has been shown to affect sleep architecture, i.e. the amount of slow-wave sleep (Kecklund & Åkerstedt, 2004; Vandekerckhove et al., 2011), REM sleep and the number of awakenings (Vandekerckhove et al., 2011). On the other hand, actigraphy has been found to overestimate the total sleeping time (Paquet, Kawinska, & Carrier, 2007; Van de Water et al., 2011) which emphasizes the finding of shortened sleep duration in this study (Study I) sample implying the sleep duration might have been even shorter.

This study has some limitations that must be addressed. For instance, the sample of nursing employees resulted in a reduced variance in job strain and therefore reduced the power to establish clear cut differences between the job strain groups. The job strain groups did not differ in levels of stress to the extent that they do in studies on the general population or diverse occupational groups. In particular, finding few group level differences in biomarkers of stress reflect the generally small

differences between the high and low job strain groups within a single occupational group.

Although the exposure data was derived from a prospective data set, the study design for analysing the associations of job strain with the study variables was cross-sectional. This prevents us from drawing conclusions regarding causality. Making general inferences of the results may be limited to the health care sector and organizations with similar amounts of working hours and similar shift schedules.

The JCQ was used to assess job strain at one particular time point, thus preventing following the changes in exposure to environmental job strain. The JCQ specifically assesses job strain and therefore the method may not capture spillover stress. However, the job strain groups did not differ with respect to family care-giving responsibilities and stressful life events. Moreover, in another Finnish study (Pennonen, 2011), there were no associations between the need for recovery and time spent on household activities. Using only three of the five JD items could also be regarded as a limitation, but JD scales with at least three items have a high correlation ( $r > 0.90$ ) with the full scale (Fransson et al., 2012b).

It must also be regarded as a limitation that one third of the contacted health-care staff refused to participate in the study and only about one fourth of the employees that fulfilled the inclusion criteria participated. This was partly due to the lack of personal contact with the potential study participants, which meant that it could not be verified whether the persons were actually reached or not. A somewhat greater proportion of volunteers was from the LJS group, and it is likely that precisely those individuals mostly affected were unwilling to participate (Barr, Spitzmuller, & Stuebing, 2008). This may have diluted the differences observed between the job strain groups.

Using the wards' average job strain level can also become a potential weakness when the atmosphere in the workplace is affected by influential individuals in the ward. However, it is unlikely that the atmosphere in the workplace noticeably affects group differences in job strain level. There were more nurses than nursing assistants in this study sample, especially in the low job strain group. This may affect the results because nursing assistants, compared to nurses, carry out more physically demanding tasks, for example, more patient transfers.

The participants were not screened for sleep disorders. An upper limit for BMI was set to minimize the probability of participants with non-diagnosed sleep apnea (Bixler et al., 2001). Nevertheless, there is a possibility that some of the participants had a shift work disorder (SWD). SWD refers to sleepiness and performance impairment during the biological night and insomnia during the biological day. The average prevalence of shift work disorder is 8–10% (Åkerstedt & Wright, 2009), but among nurses prevalence up to 32–38% has been found (Flo et al., 2012).

Due to practical reasons, there was only one assessor of the TSST, whereas the standard protocol uses three assessors (Kirschbaum et al., 1993). The cortisol responses to the TSST might have been more explicit if the test had included three assessors. The lack of information concerning the participants' menopausal status is also a limitation, since after the menopause acute sympathoadrenal responsiveness increases (Kajantie & Phillips, 2006).

### 9.3 Practical implications

An empirical study design embedded in an epidemiological research can provide more valuable information about the associations of job strain, sleep and stress biomarkers in employees on shift work. The results of this study can be used in shift planning and in occupational health and safety education within the health care sector. For example, the findings are consistent with the notion that ergonomics in shift planning can be improved by reducing backward rotating shift schedules with quick returns to a morning shift after an evening shift; that adequate inter-shift recovery should be promoted by reducing single days off; and that the importance of sufficient sleep should be made clear to all shift workers (Flo et al., 2013; Garde et al., 2012; Hakola et al., 2010; Sallinen & Kecklund, 2010; Åkerstedt & Wright, 2009). Especially in the case of high job strain, scheduled naps may be useful prior to the first night shift and, when appropriate, also during the night shift (Bonnefond et al., 2001; Davy & Gobel, 2013; Ruggiero & Redeker, 2014; Tremaine et al., 2013). According to the results, increased attention should also be paid to the reduction of physical workload, especially among employees with a high job strain.

High job strain should be reduced both at the organizational and individual level, as job strain is associated with difficulties in sleep and maintaining alertness, which may reduce occupational and patient safety (Scott et al., 2010). Job strain among nursing professionals could be reduced by increasing the employees' influence on their working times and work content, i.e. increasing job control (Ala-Mursula et al., 2002; Takahashi et al., 2012). As staff retention and intentions to leave the profession are common in the health care sector (Aiken et al., 2013), increasing job control might facilitate staff recruitment and reduce turnover. At the individual level, nursing professionals might benefit from cognitive-behavioural stress management intervention (Ruotsalainen et al., 2014) as well as educating staff about other fatigue countermeasures in addition to napping (Scott et al., 2010). However, further intervention studies are needed to confirm these recommendations.

### **9.4 Implications for future research**

The author's presentation of a "Model of shift work, job strain, sleep and early signs of negative health effects" was supported by results of disturbed sleep and poor recovery, but not by psychophysiological changes. Increased understanding of the interactions between shift work, job strain and sleep is needed, and progress will most likely be achieved from longitudinal studies on work stress in real-life situations (Åkerstedt, 2006). For example, longitudinal studies exploring the effects of long-term job strain on the health and well-being of shift workers are needed, as well as studies on sleep quality and shift schedules among major occupations and different age groups.

Future sleep studies would benefit from the detection of sleep architecture with EEG-based measurements. Individual fatigue countermeasures such as taking breaks (Driskell & Mullen, 2005) were not included in this study, and the effects of countermeasures on alertness and sleepiness should be subject to further studies. Giving up night shift work altogether was common within the sample group from which the participants were recruited, hence it would be advantageous to also include ex-shift workers in future studies.

To collate more comprehensive data on working times and shift schedules, a longer study period with completed rosters would be useful. As sleep difficulties, sleepiness and poor recovery were especially associated with evening shifts and quick returns, these shifts and shift combinations would probably be prone to show job strain induced changes in psychophysiological recovery too. Among the different health care occupations there is a lack of knowledge about sleep and shift work particularly among paramedics (Sofianopoulos, Williams, & Archer, 2012) and home health care workers (Lamberg, 2004). There is also a need for high-quality stress and sleep management interventions among shift working health care personnel (Hasson & Gustavsson, 2010; Ruotsalainen et al., 2014).

Analysing group level differences in HRV was as challenging as in previous studies (Järvelin-Pasanen et al., 2013; Riese et al., 2004; Uusitalo et al., 2011; Yoshizaki et al., 2013). However, to gather group level differences, a larger sample size and better control over leisure and work time activities would be advantageous. To avoid random positive group differences in multiple HRV comparisons bootstrapping is recommendable statistical method in future studies. Likewise, as in previous studies (Kidd, et al., 2014; Wingenfeld et al., 2010; Wong et al., 2012), this study also included a single measurement day per shift. It would be recommendable to collect several days' saliva samples for each measurement or shift type. Preferably a better control of pre-measurement activities for cortisol and timing of meals for alpha-amylase would also be advantageous. Narrowing the time frame of evening saliva sample collection would possibly reduce variations in the results (Marchand et al., 2014). This study provided a unique opportunity to study stress biomarkers, both in a laboratory stress reactivity test and in field conditions. Despite the minor stress induced changes in the results of this study, the combination of laboratory and field measurements would be worthy off further research. Laboratory stress tests are assumed to reflect the way individuals react in real life (Kidd et al., 2014) and confirming this assumption could be taken into account in future study protocols.

## **10 MAIN FINDINGS AND CONCLUSIONS**

This study has its strengths in its ward-level measurements of exposure to a stressful work environment; use of a study sample recruited from a large epidemiological study; use of a measurement protocol which was similar for all participants with respect to circadian rhythm and recovery time; and the collection of working time data from completed rosters. However, focusing on health care professionals only reduced variance in job strain and therefore reduced the power of establishing clear cut differences between the job strain groups. Although the job strain exposure data was from a prospective data set, the cross-sectional study design prevented the drawing of conclusions regarding causality.

The main findings and conclusions of the present thesis can be summarized as follows:

1. Shift working contributed to impaired sleep in both high and low job strain groups. The sleep impairment was more evident within the high job strain group in connection to sleep before a morning shift and after an evening shift as well as in napping before the first night shift. Sufficient and good quality sleep is crucial for all shift workers because of its implications for alertness, recovery and health.
2. In this study, high job strain was not associated with extended working hours. Severe sleepiness and poorer recovery in the high job strain group were at least partly attributable to more common unfavourable shift arrangements in this group, for example, quick returns and single days off.

## 10 MAIN FINDINGS AND CONCLUSIONS

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3. The findings suggest that reducing the number of quick returns and single days off, and thus increasing time for recovery, can be effective in reducing job strain and improving sleep quality among shift workers.
4. Within this sample, exposure to a stressful work environment was associated only with minor psychophysiological stress-related reactions and changes in biomarkers of stress during the day-time and in heart rate variability during sleep.

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Psychosocial factors have emerged as an occupational health issue. Stress is associated with various symptoms such as sleep disturbances and gastro-intestinal problems, and, in the long term, diseases such as depression and coronary heart disease. Prevalence of occupational stress is one of the highest in health care sector compared to other sectors. Among health care staff irregular working hours and stressful work may challenge employees' possibilities to sleep and recover sufficiently. Sleep is essential for the recovery from job strain, but job strain may impair sleep more among shift workers than day workers, because shift workers are also exposed to circadian misalignment. The aim of this study was to extend the knowledge on job strain and shift work by examining the association of job strain with sleep and psychophysiological functioning and recovery among shift working health care professionals in laboratory and field.

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